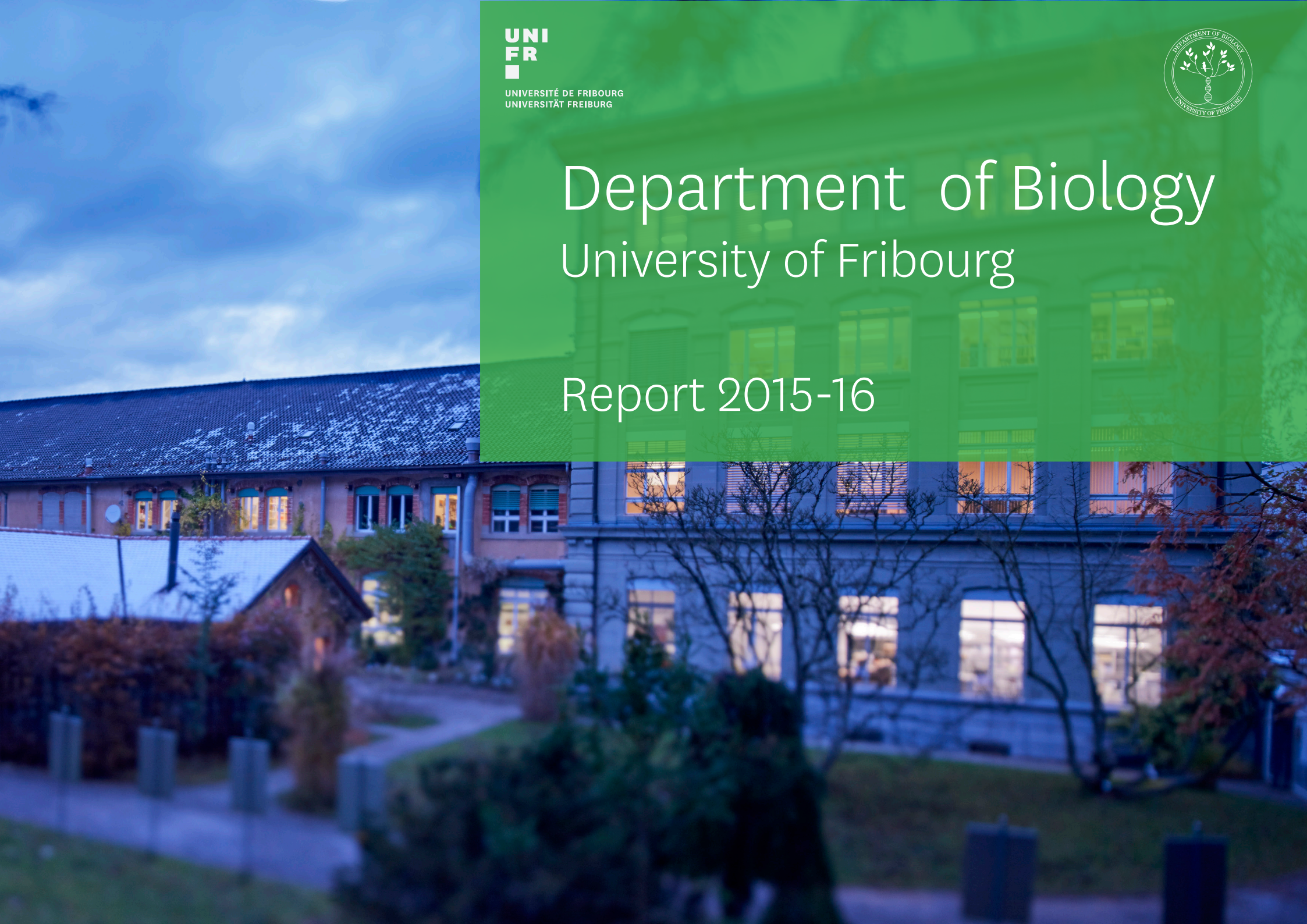


Department of Biology University of Fribourg

Report 2015-16





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A man with short dark hair, wearing a light blue button-down shirt, stands with his arms crossed in a laboratory setting. He is wearing a watch on his left wrist. The background is filled with laboratory equipment, including shelves with numerous clear plastic bottles with blue caps, and pipettes hanging from a rack. The scene is brightly lit, typical of a modern research facility.

**Welcome from
the President**

Life science is rapidly evolving. Over the past decades particularly technical advances revolutionized the possibilities at multiple scales of how “life” can be studied. While 20 years ago it took years to sequence a single gene, it is today possible to sequence entire genomes in a few days. Similarly, while it was impossible to capture cellular processes in real time, today new imaging techniques enable us to see and visualize biological processes as they happen. This rapid expansion of research in Biology comes with a range of possibilities, but also challenges. For instance, an increasing number of students, higher costs for experiments and more expensive infrastructure. The Department of Biology has a strong commitment to provide an outstanding research environment with strong dedication for excellent teaching. To achieve this in a most effective and productive fashion the Department has undergone some major change in its organization. The former “units” have disappeared allowing a wide, flexible organization of the Department with a flat hierarchy. The reorganization allows us to jointly share all experimental machines, apparatuses infrastructures easily and efficiently. To support research and teaching we have recently introduced platforms that are aimed to be functioning interdepartmentally with other research groups in the faculty that have similar interests and needs. We have established platforms in “Bioinformatics”, “Bioimaging” and “Proteomics and Metabolomics”. Also, the Botanical Garden is an important part of the Department providing platform-services to students and researchers. Importantly, we have initiated a more flexible organization of the Biology Master program, offering students a range of offered specializations. This updated organization allows students to choose specializations in the area and field they are most interested in.

President of the Department of Biology
Prof. Simon Sprecher



Platforms

A photograph of a laboratory environment. In the foreground, a person in a white lab coat is seated, facing away from the camera towards a computer monitor. In the middle ground, a woman with brown hair and glasses, wearing a white lab coat, is seated on a black swivel chair at a desk, smiling and looking towards the left. In the background, a man with dark hair and glasses, wearing a white lab coat, is standing and using a blue pipette to transfer liquid into a small vial. The lab bench is cluttered with various items, including a large brown bottle with a red cap and a label, a small beaker, and some boxes. A sign on the wall in the background reads "Windows must not be opened!". The word "Platforms" is overlaid in a large, green, sans-serif font on the right side of the image.

The Bioinformatics Core Facility has been established in 2013 as a joint platform between the Departments of Biology and Medicine. It is managed by Dr Laurent Falquet.

The expertise of the platform is primarily the analysis of Next Generation Sequencing data, with emphasis on genome assembly and comparative genomics, as well as DNA methylation.

We also perform various analyses like RNAseq, ChIPseq, metagenomics, etc... For more details see page 22.

Please contact us at bugfri@unifr.ch

The Proteomics/Metabolomics Core Facility has been established in 2016. It is managed by Prof. Jörn Dengjel (Coordinator), Dr Laurent Méne-Saffrané (Metabolomics) and Dr Dieter Kressler (Proteomics).

We are using liquid chromatography coupled to high-accuracy, high-resolution mass spectrometry to identify and quantify biomolecules. In proteomics the analysis of peptides and the characterization of their posttranslational modifications, such as phosphorylation, is the focus. In metabolomics we quantify small molecules and lipids.

Please contact us at joern.dengjel@unifr.ch

The BioImage Light Microscopy Facility has been established in 2013 as a joint platform between the Departments of Biology and Medicine. It is managed by Boris Egger (coordinator Department of Biology), Felix Meyenhofer (platform engineer) and Christophe Lamy (coordinator Department of Medicine).

Currently, Bioimage Unifr is attended by 112 active users coming mainly from the Departments of Medicine and Biology and a few researchers from the Adolphe Merkle Institute (AMI) and the Department of Physics. Bioimage maintains a comprehensive set of high quality optical imaging systems and software for image analysis. The facility provides training in using the instruments on the platform and runs teaching courses in light microscopy and image processing for life sciences.

For further details consult <http://www3.unifr.ch/bioimage/>

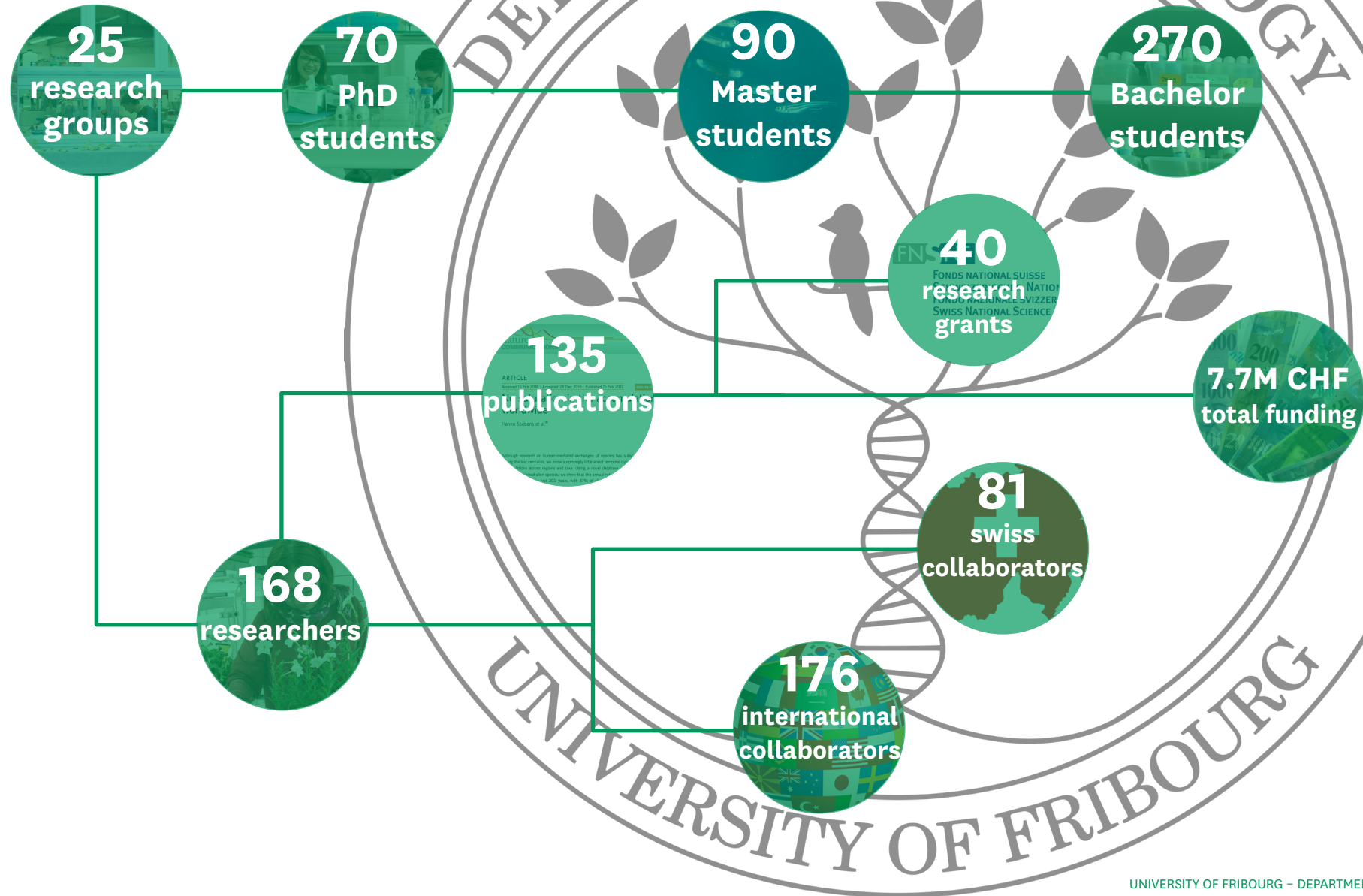
The Botanical Garden has been established in 1937. It is managed by Prof. Gregor Kozłowski (curator) and Nicolas Ruch (technical manager).

The Botanical Garden is a living museum and a competence center for conservation of rare and threatened plants. Its scientific, well-documented collections count more than 5'000 plant species cultivated in 21 sectors, including 3 greenhouses. The Botanical Garden, besides its participation in teaching and research, serves as a platform for vulgarization of scientific activities of the Department of Biology. Moreover, the Botanical Garden conducts numerous scientific activities led by Gregor Kozłowski and his group in collaboration with more than 20 international and national institutions, i.e. with the Natural History Museum Fribourg (NHMF).

For further details consult <http://www3.unifr.ch/jardin-botanique>

The Department in numbers

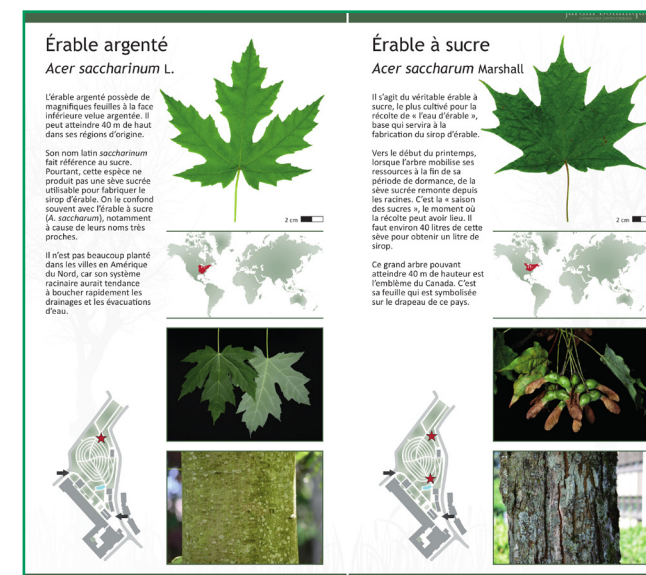
During the years 2015/16 the Department of Biology had ...





The Botanical Garden: an open-air laboratory for life sciences

Founded in 1937 and serving at the beginning only students of medicine and pharmacy, the Botanical Garden of the University of Fribourg opened to the public in 1948. Today, its scientific, well-documented collections count more than 5'000 plant species cultivated in 21 sectors, including 3 greenhouses. The Botanical Garden is a pleasant place to relax, but above all, it is a living museum and a competence centre for conservation of rare and threatened plants. Furthermore, public awareness and popularization of science are important missions of the Botanical Garden. Moreover, Botanical Garden conducts numerous scientific activities led by Gregor Kozłowski and his group in collaboration with more than 20 international and national institutions, i.e. with the Natural History Museum Fribourg (NHMF). More information under <http://www3.unifr.ch/jardin-botanique>



Botanical Garden regularly publishes books and brochures, making its scientific collections as well as various biological and botanical topics accessible to students and to the large public.

The illustration shows two selected pages from the book published in autumn 2016 presenting all 22 species of maples (*Acer* sp., family Sapindaceae) cultivated in the Botanical Garden.

Co-workers

Prof. Gregor Kozłowski (Curator), Yann Fragnière (Scientific collaborator), Nicolas Ruch (Technical manager), Benoît Clément, Marianne Herren, Hélène Huguet-Sahli, Christine Jakob, Manuela Moduli, Josef Schöpfer, Jacques Sciboz, Hans Tschachtli, Justine Alvazzi, Martin Huber.

Selected publications

Fragnière Y, Kozłowski G. (2016) Les érables du Jardin botanique de Fribourg / Ahorne des Botanischen Gartens Freiburg. Botanical Garden of the University of Fribourg, Switzerland. pp. 32.

Gratzfeld J, Kozłowski G, Fazan L, S. Buord, Garfi G, Pasta S, P. Got-siou, Fournaraki Ch, Dimitriou D. (2015) Whither rare relict trees in a climate of rapid change? BGjournal 12.2.: 21-25.



Research





Prof. Urs Albrecht

Chronobiology

Circadian clock, sleep, mood-environmental adaptation

Is the healthy circadian clock the secret of good mood and health ?

The Albrecht lab investigates circadian clocks in mammals. Circadian clocks organize an organism's daily behavior and physiology on a 24-hour time scale. These 24-hour rhythms are pervasive at all levels of organization, from complex behavior to organ specific function down to the scale of autonomous cellular oscillations. The timing in mammals is organized hierarchically, with a master pacemaker in the suprachiasmatic nuclei (SCN) controlling subordinate central and peripheral clocks making up the circadian system. This system is tuned to the environment via light and food. Drugs like alcohol and cocaine can interfere with these environmental stimuli leading to misalignment of the circadian clock with the day/night cycle.

We are interested in the question how clocks in different tissues adjust to environmental cues and how the brain integrates this information to produce coherent systemic circadian rhythms as observed in food anticipation, drug seeking and metabolic rhythms. This is of central interest, because loss of a stable clock-phase relationship between organs is one of the characteristics found to be altered in many human diseases including depression, obesity and cancer.

Co-workers

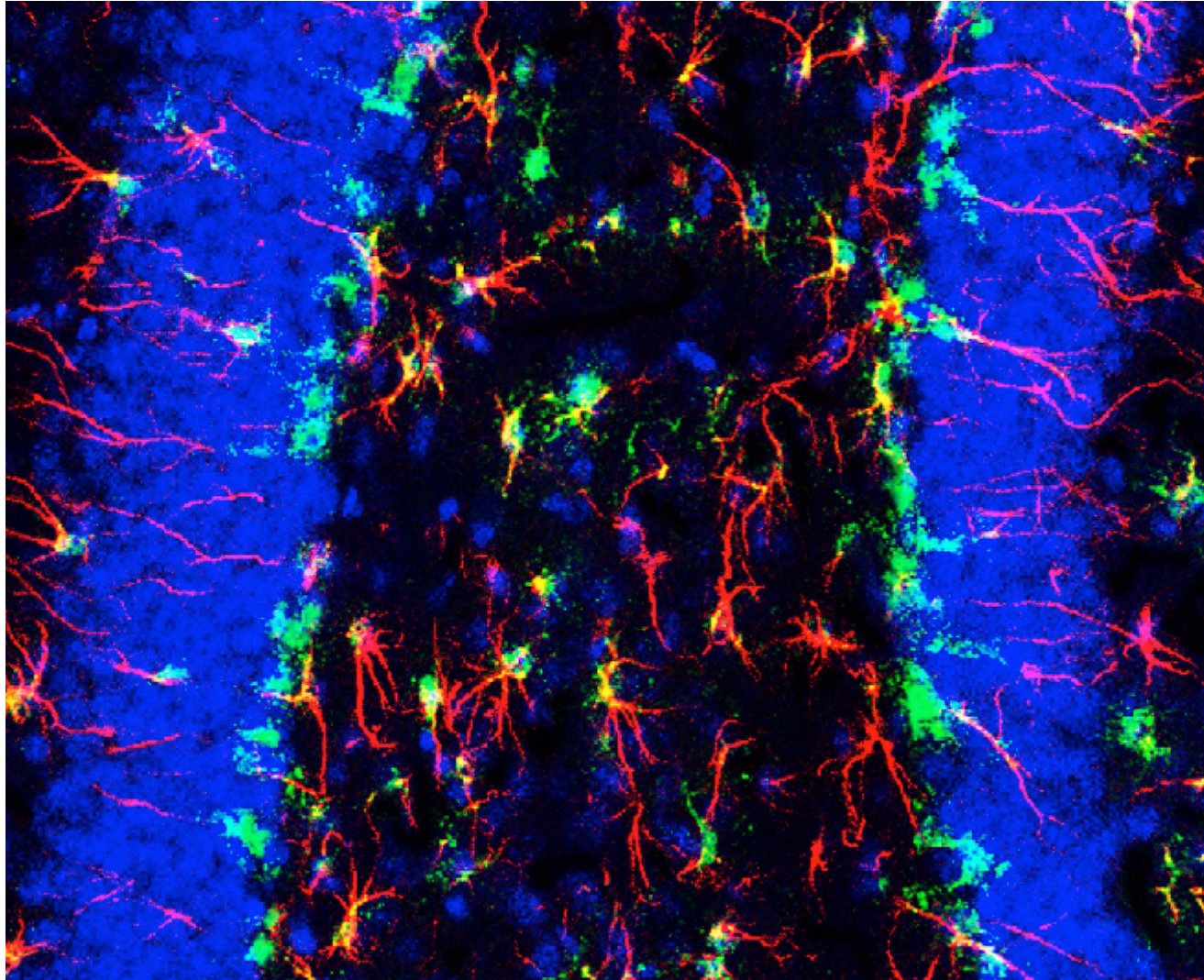
Dr Jürgen Ripperger, Dr Andrea Brenna, Dr Rohit Chavan, Iwona Olejniczak, Tomaz Martini, Emilie Cropt, Stéphanie Baeriswyl-Aebischer, Antoinette Hayoz, Ashot Sargsyan.

Selected publications

Chavan R. et al. (2016) Liver-derived ketone bodies are necessary for food anticipation. *Nat. Comm.* 7: 10580.

Schnell A. et al. (2015) Mice lacking circadian clock components display different mood-related behaviors and do not respond uniformly to chronic lithium treatment. *Chronobiol. Int.* 32: 1075-1089.

Schnell A. et al. (2014) The nuclear receptor REV-ERB α regulates *Fabp7* and modulates adult hippocampal neurogenesis. *PLoS One* 9: 6, e99883. 1.



The nuclear receptor REV-ERB α regulates Fabp7 and modulates adult hippocampal neurogenesis. Confocal microscopy image of the hippocampal dentate gyrus of Rev-erba knock-out mice. Neuronal precursor cells are labelled with anti-FABP7 antibody (green), radial glia cells are visualized with an anti-GFAP antibody (red) and cell nuclei are stained with DAPI (blue).

Photo: A. Schnell.

Ongoing and future projects :

Influence of light on brain clocks and mood related behavior in mice. Certain forms of depression can be successfully treated with light therapy. However, the mechanism how this works is unknown. We aim to identify mechanisms explaining how light affects brain function relevant for mood regulation. For this purpose we use mice as a model system. Functions of neurons and astrocytes in mood related behavior. We generated mice which lack the clock gene Per2 in neurons or in astrocytes. This enables us to test the functions of this clock gene in a cell type specific manner to elucidate the neuronal and astrocytic contributions to the regulation of mood-related behaviors in mice.

Funding Source: Swiss National Science Foundation and Velux Foundation.

Which is the worst invasive alien species ?



Prof. Sven Bacher

Applied ecology

Biological invasions, biodiversity and biological control

The number of alien species is increasing exponentially world-wide and there are many more species than can be managed. In Europe alone, more than 14000 alien species are known, but not all of them cause problems to the environment or human well-being. The seemingly simple and straightforward question “which are the worst invaders?” is difficult to answer because the impacts of alien species can be manifold and comparisons need to work for species as different as for example snails, insects, mammals and plants. However, such a methodology is urgently needed by policy makers.

In an international team, we recently developed a system that allows classifying alien species according to the magnitude of their environmental impacts (EICAT), based on the mechanisms of impact used to code species in the International Union for Conservation of Nature (IUCN) Global Invasive Species Database. The system has been recently endorsed by the IUCN as international standard (<https://portals.iucn.org/congress/motion/014>).

Co-workers

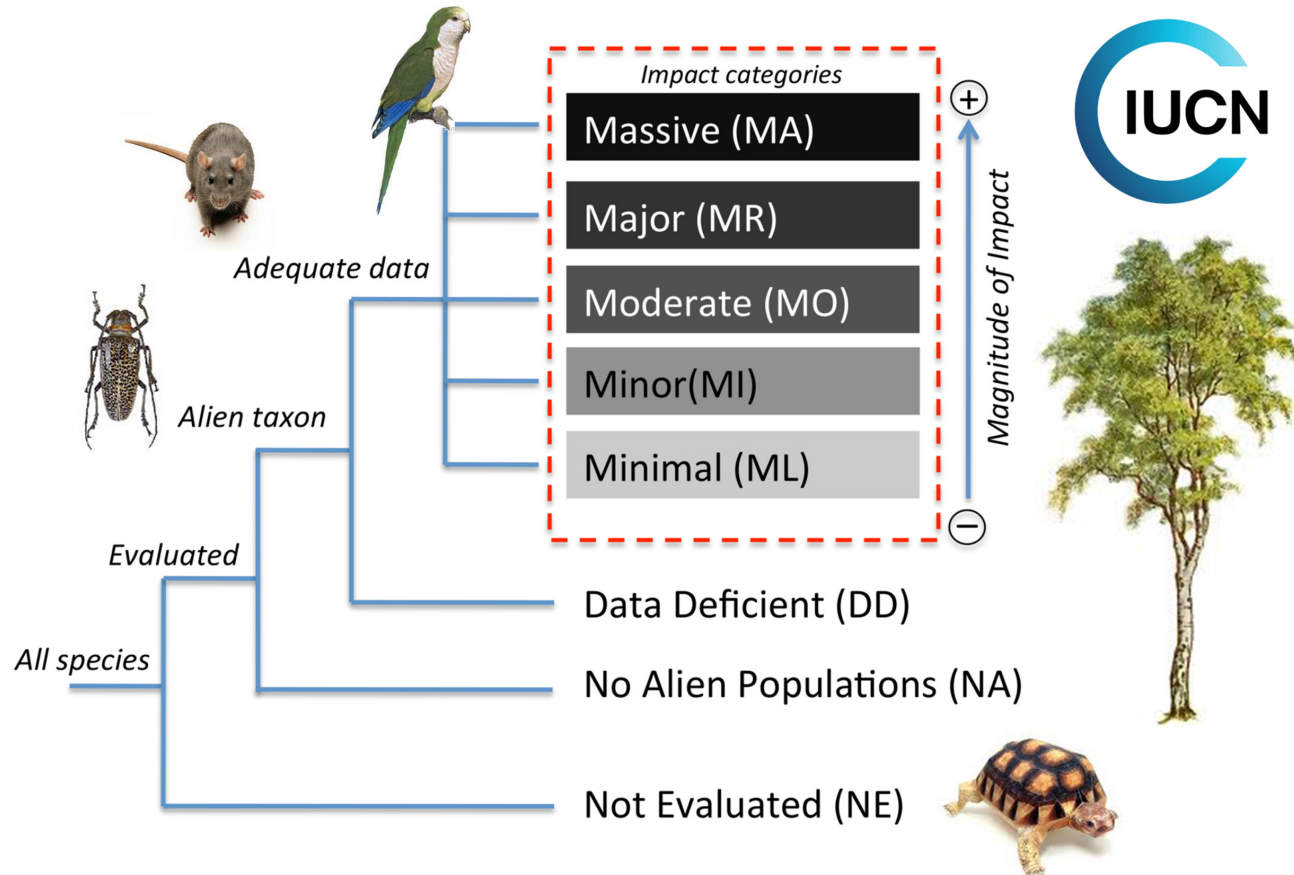
Silvia Rossinelli, Magdalena Steiner, Sonja Eckard, Deborah Kaiser, Andrea Zanetta, Anne-Laure Fragnière, Franziska Keller, Baptiste Michel, Divija “DJ” Jatavallabhula, Lara Volery, Andy Brown, Mervi Laitinen, Susan Apebende, Nina Häner

Selected publications

Kumschick S et al. (2015) Comparing impacts of alien plants and animals in Europe using a standard scoring system. *J Appl Ecol* 52: 552-561

Hawkins CL et al. (2015) Framework and guidelines for implementing the proposed IUCN Environmental Impact Classification for Alien Taxa (EICAT). *Div Dist* 21: 1360-1363

Blackburn TM et al. (2014). A Unified Classification of Alien Species Based on the Magnitude of their Environmental Impacts. *PLoS Biol* 12(5): e1001850.



Can we improve wine quality with biodiversity?

Wine growing aims at maximising wine quality, not quantity. Therefore vineyards do not require massive resource inputs and provide ideal growing systems to combine high levels of biodiversity with agriculture. It is known that biodiversity improves ecosystem functions, but practical applications are rare.

In the European project PromESSinG (www.promessing.eu) we investigate how we can use biodiversity-friendly agricultural management techniques to improve grape quality. We show that permanent vegetation cover improves soil microbial biodiversity and ecosystem functions such as soil activity and that this leads to changes in grape sugar, acid and nitrogen content. This information can be used by wine growers to improve the quality of their wines.



Prof. Louis-Félix Bersier

Community ecology

Community structure and functioning

Can microbial communities reveal the effects of global warming on natural communities?

Natural communities are composed of a myriad of species interacting in many ways between themselves and with their physical environment. Their action is essential as communities deliver "ecosystem services" like food provisioning, carbon sequestration, or nutrients recycling. How can global change affect the structure and functioning of communities? This is a very complex question as temperature affects many aspects of the community, from individual metabolic rates to habitat quality. We chose to tackle this question by working with simple natural systems: the microbial food webs inhabiting the pitcher-shaped leaves of *Sarracenia purpurea*, a carnivorous plant. This system is simple enough to be captured in mathematical models and to be amenable to replicated experiments, but complex enough to reflect larger-scale systems.

We conducted several experiments in incubators to test the effect of temperature change on various aspects of community organisation. Notably, we performed several experiments in Canada with North American and European communities to explore the possible adaptation to new biotic and abiotic environments.

Co-workers

Prof. Roger Ardit, Anthony Balet, Bastien Boschung, Dr Sarah Gray, Christell Imhof, Elodie Parain, Dr Rudolf Rohr, Nadine Sandau, Axel Zander

Selected publications

Parain EC, Gravel D, Rohr RP, Bersier L-F, Gray SM (2016) Mismatch in microbial food webs: predators but not prey perform better in their local biotic and abiotic conditions. *Ecology and Evolution* 6(14): 4885–4897.

Zander A, Bersier L-F, Gray SM (2017) Effects of temperature variability on community structure in a natural microbial food web. *Global Change Biology* 23(1):56-57.

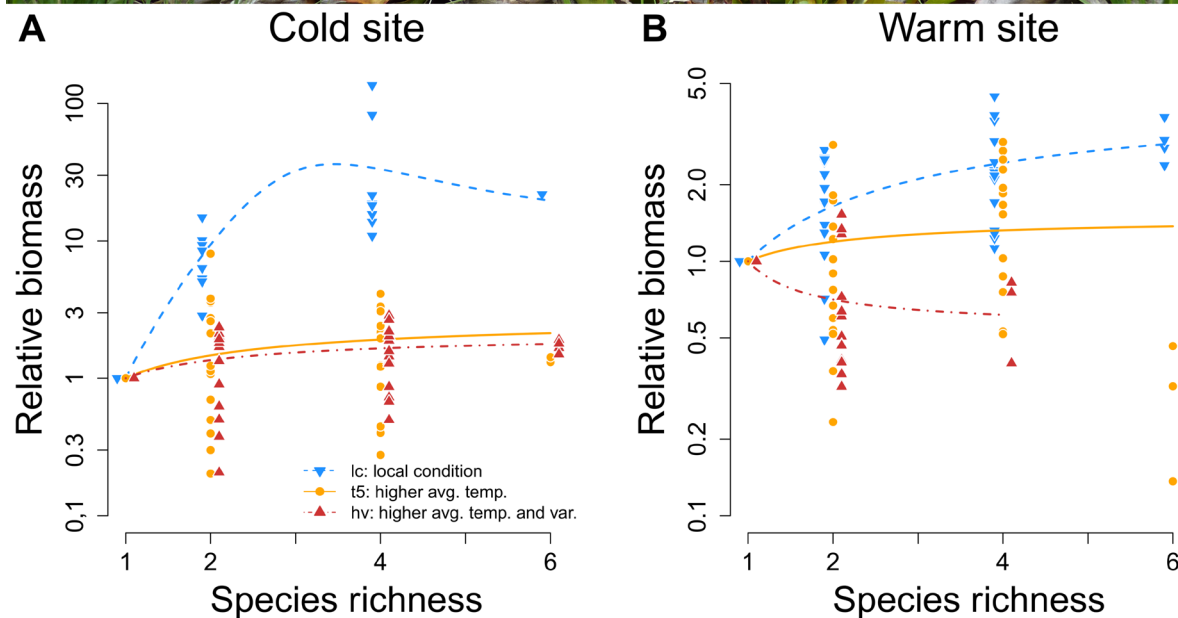
Sandau N, Fabian Y, Bruggisser OT, Rohr RP, Naisbit RE, Kehrli P, Aebi A, Bersier L-F (2016) The relative contribution of species richness and species composition to ecosystem functioning. *Oikos* 000: 001–010.



From conservation to theoretical questions

We worked on the relationship between biodiversity (species richness) and ecosystem functioning (measured as biomass production) in grasslands and with the microbial systems. With the latter, we built a theory for the effect of temperature on this relationship, which predicts that increased temperature should weaken the positive effect of biodiversity on biomass production, and even make this relationship negative (see figure).

We worked on other aspects of community ecology. For example, we studied the effect of beaver dams on aquatic insects; we tackled fundamental theoretical questions like the relationship between the pattern of abundance in communities and their productivity and dynamical stability.



Sarracenia purpurea (Top). Increasing temperature (experimental temperature increases from blue to orange to red) weakens the positive effect of species richness on biomass production of protists inhabiting the *Sarracenia* leaves and even makes it negative in the warm site (Bottom).



Prof. Jörn Dengjel

Protein Homeostasis

Proteomics/metabolomics
core facility

How does cellular recycling work ?

We are interested in protein homeostasis and its regulation.

Specifically, we study the role of the extracellular matrix and of the intracellular degradation pathway autophagy in regulating protein homeostasis. Autophagy is a cellular degradation pathway involved in ageing and numerous diseases, amongst others in cancer and neurodegenerative disorders. We address questions like: how are proteins selected to be degraded by autophagy and which are the underlying signaling events? With respect to the extracellular matrix, we are interested in the function and regulation of collagen VII, a structural protein important for epidermal-dermal adhesion. Mutations in the gene encoding collagen VII, COL7A1, cause the inherited skin disease dystrophic epidermolysis bullosa for which no cure is available. We develop mass spectrometry (MS) approaches to analyze the dynamics of protein-protein interactions and posttranslational modifications. Using quantitative MS-based proteomics we study the cellular microenvironment, organellar protein dynamics, signaling kinetics and protein turnover with the aim to reveal molecular mechanisms deregulated in disease.

Co-workers

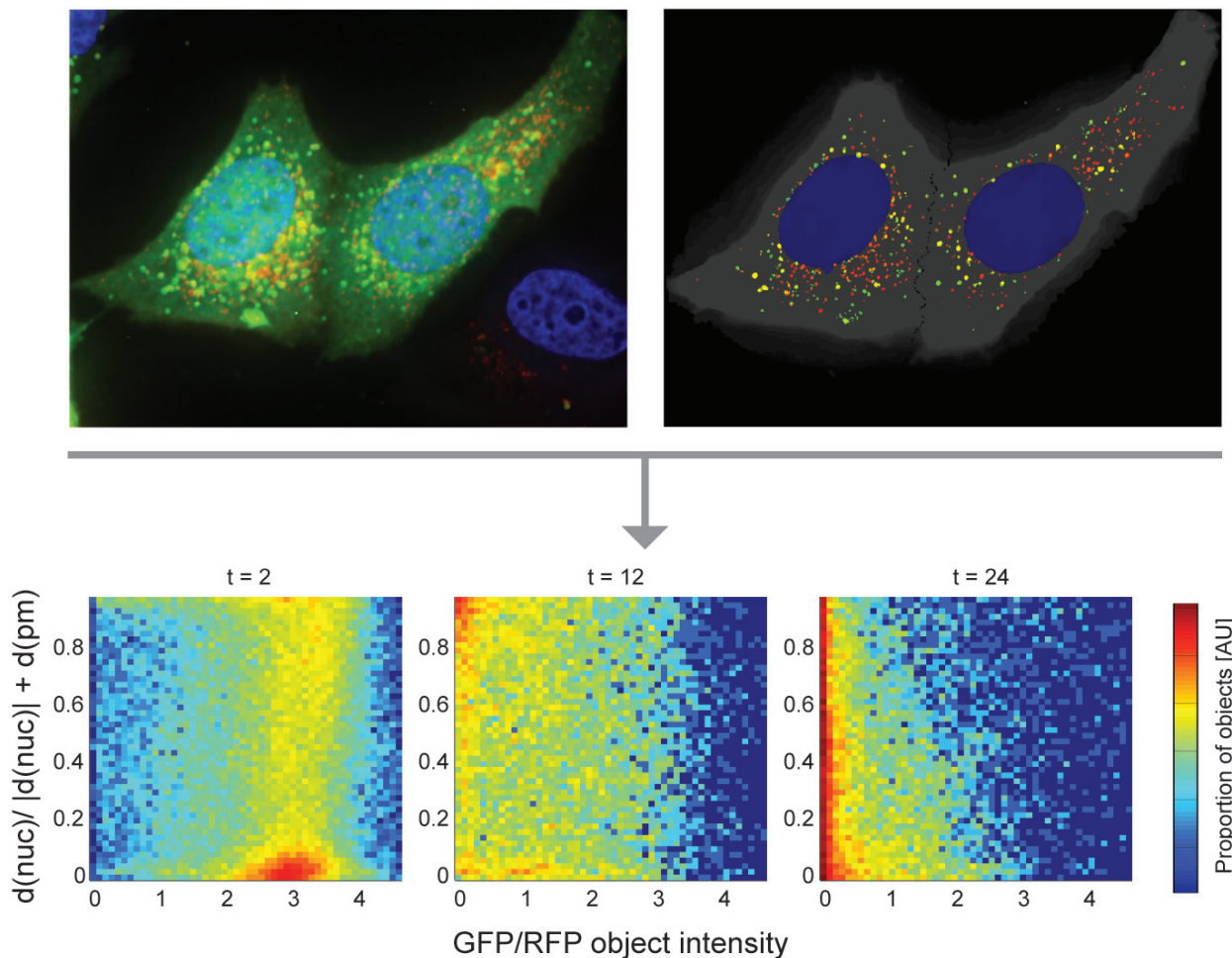
Dr Stéphanie Kaeser-Pebernard, Dr Britta Diedrich, Zehan Hu, Michal Rackiewicz, Carole Roubaty, Christine Vionnet, Kerstin Thriene, Regine Tölle, Jianwen Zhou

Selected publications

Diedrich B, Rigbolt KT, Röring M, Herr R, Kaeser-Pebernard S, Gretzmeier C, Murphy RF, Brummer T, Dengjel J. (2017) Discrete cytosolic macromolecular BRAF complexes exhibit distinct activities and composition. EMBO. doi: 10.15252/embj.201694732

Gretzmeier C, Eiselein S, Johnson GR, Engelke R, Nowag H, Zarei M, Küttner V, Becker AC, Rigbolt KT, Høyer-Hansen M, Andersen JS, Münz C, Murphy RF, Dengjel J. (2017) Degradation of protein translation machinery by amino acid starvation-induced macroautophagy. Autophagy. in press.

Abeliovich H, Zarei M, Rigbolt KT, Youle RJ, Dengjel J. (2013) Involvement of mitochondrial dynamics in the segregation of mitochondrial matrix proteins during stationary phase mitophagy. Nat Commun. 2013;4:2789.



Addressing a more fundamental question, we ask if and how eukaryotic cytosol is compartmentalized.

For this we use a combination of MS-based proteomics methods and fluorescence imaging. Combining information about protein-protein interactions, the spatial organization of multi-protein complexes and advanced image processing we develop assays to map and study the regulation of macromolecular protein assemblies in cell stress.

Autophagosome localization and turnover between plasma (pm) and nuclear (nuc) membrane is depicted employing GFP/RFP ratios. The y axis depicts the distance between nuclear and plasma membrane, 0 being at the nuclear membrane and 1 at the plasma membrane.

The ins and outs of quiescence in yeast



Prof. Claudio De Virgilio

Nutrient signaling
and control of quiescence in yeast

All living cells are capable of exiting the normal cell cycle and entering an alternative resting state termed quiescence or G_0 . Despite the fact that most eukaryotic cells, whether they exist as single cells or as part of a multi-cellular organism, spend most of their life in a quiescent state, relatively little is known about the regulatory mechanisms that control entry into or exit from such a state. The available body of data, nevertheless, indicates that disruption of G_0 -entry/exit control mechanisms is often associated with either cellular transformation (in multi-cellular organisms), or dramatically reduced life span (particularly in unicellular organisms). In this context, our research is focused on the elucidation of the conserved mechanisms controlling entry into, survival in, and exit from G_0 . We anticipate that our experimental approaches may not only enhance our basic understanding of diseases such as cancer or premature aging, but also provide a basis for the development of diagnostic and therapeutic tools to treat cancer and prolong life.

Co-workers

Dr Marie-Pierre Péli-Gulli, Dr Riko Hatakeyama, Dr Ladislav Dokládál, Dr Raffaele Nicastro, Alessandro Sardu, Serena Raucci, Guillermo Miguel García Osuna, Malika Jaquenoud, Floriane Jaquier

Selected publications

Powis, K., and De Virgilio, C. (2016). Conserved regulators of Rag GTPases orchestrate amino acid-dependent TORC1 signaling. *Cell Discov.* 2: 15049.

Péli-Gulli, M.-P., Sardu, A., Panchaud, N., Raucci, S., and De Virgilio, C. (2015). Amino acids stimulate TORC1 through Lst4-Lst7, a GTPase activating protein complex for the Rag family GTPase Gtr2. *Cell Rep.* 13(1): 1-7.

Moreno-Torres, M., Jaquenoud, M., and De Virgilio, C. (2015). TORC1 controls G1-S cell cycle transition in yeast via Mpk1 and the greatwall kinase pathway. *Nat. Commun.* 6:8256.

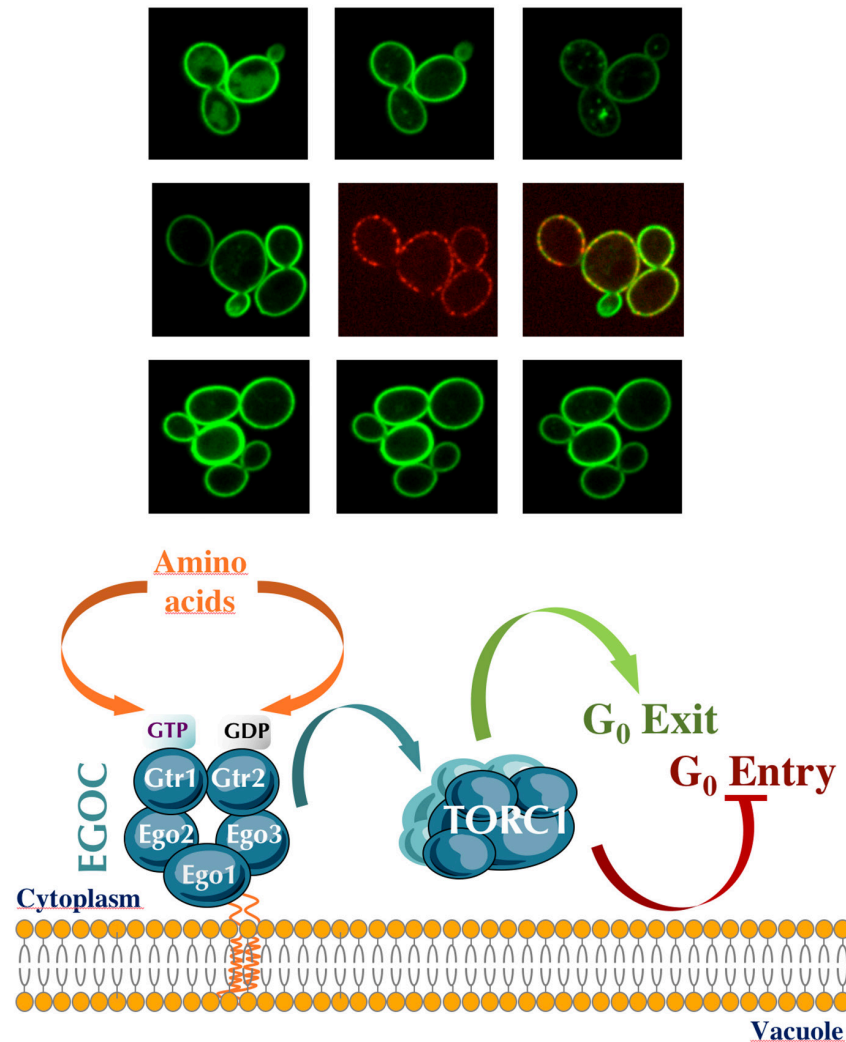


Figure 1 : (Top) The yeast *Saccharomyces cerevisiae* represents an ideal model system to study fundamental, conserved aspects of cell cycle control (during mitosis) and of developmental processes such as meiosis or entry into and exit from quiescence (G_0). (Bottom) Schematic diagram depicting our view of the function of the Rag GTPases (Gtr1 and Gtr2) within the EGO complex (EGOC). We are currently studying how amino acids are sensed by the Rag GTPases and how, in turn, these GTPases regulate TORC1. In parallel, we try to elucidate how TORC1 regulates downstream events such as entry into and exit from G_0 .

To address basic aspects of quiescence experimentally, we have chosen the unicellular eukaryote yeast *Saccharomyces cerevisiae* as a model system (Figure 1, Top). Current data indicate that a conserved protein complex, coined target of rapamycin complex 1 (TORC1), plays a central role in yeast in coordinating both entry into and exit from G_0 in response to nutrient levels. Interestingly, we discovered that amino acids represent essential and primordial signals that modulate TORC1 activity through the conserved Rag family GTPases (Gtr1 and Gtr2) within the yeast EGO complex (EGOC). We are therefore currently addressing the molecular mechanism by which Rag GTPases sense amino acids and regulate TORC1 in yeast (Figure 1, Bottom). Since some of the underlying mechanisms appear to be highly conserved, our studies may be helpful in understanding pathological conditions, including cancer, obesity, and type 2 diabetes, which are caused by deregulated TORC1 in humans.



Dr Boris Egger

Neural stem cell states
Bioimage core facility of the
University of Fribourg

Symmetric versus asymmetric divisions - when is it time to switch?

During brain development neural stem cells go through phases of cell proliferation followed by phases of differentiation. Symmetric proliferative cell divisions lead to a rapid increase in the stem cell pool while in asymmetric divisions stem cells are self-renewed and at the same time more specialized cell types are generated.

In our research we use genetics and confocal microscopy to observe the cellular and molecular mechanisms that control the transition of stem cell states in the fruit fly model *Drosophila melanogaster*.

We have recently shown that the nuclear hormone transcription factor Tailless (Tll) has a crucial role in regulating the maintenance of symmetrically dividing neuroepithelial stem cells. Mutations in the tailless gene result in cell death of neuroepithelial cells, failure in the specification of progenitor cells and the loss of neurons in all optic brain ganglia of the developing visual system.

Co-workers

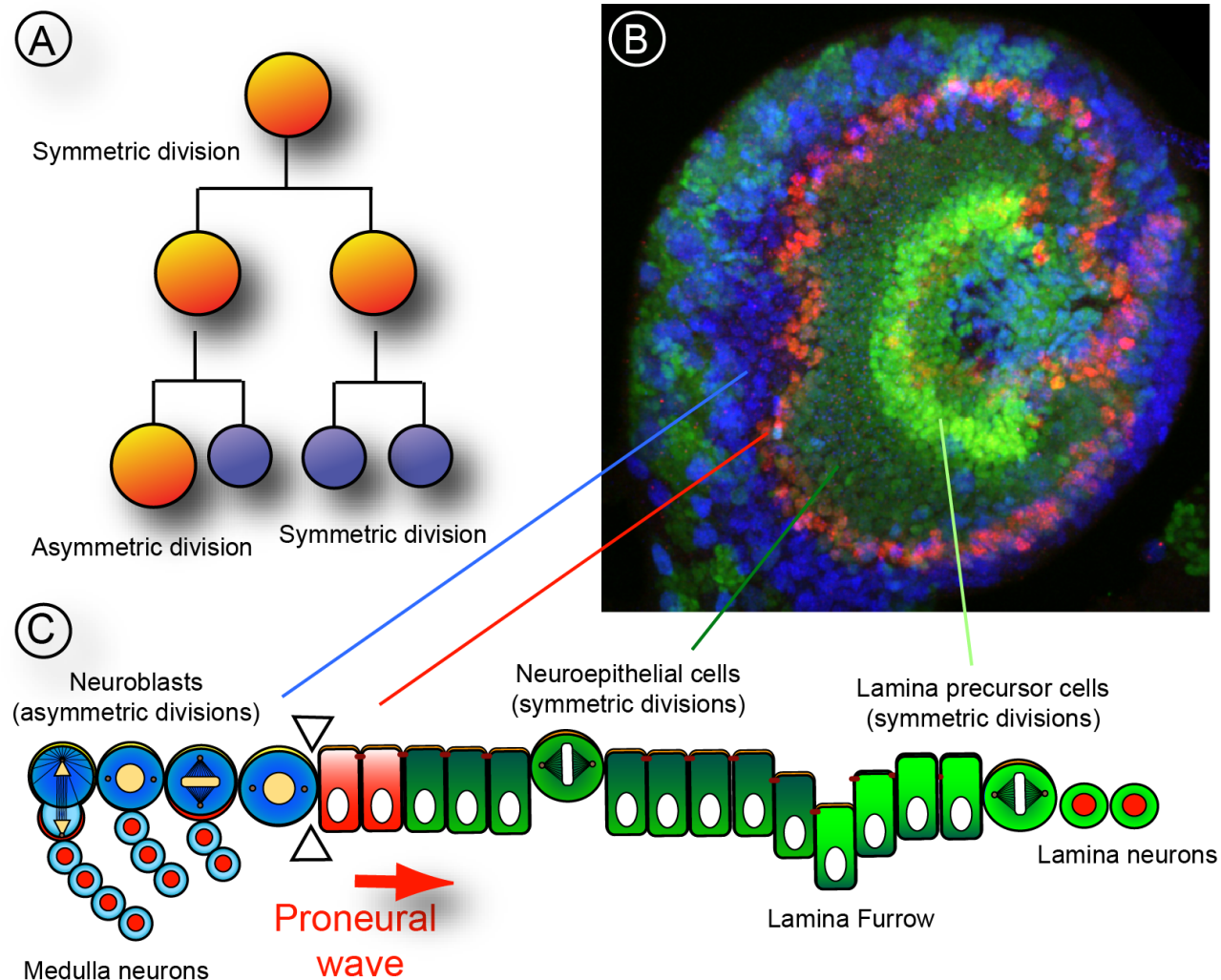
Dr Oriane Guillermin, David Rodriguez Crespo, Martin Baccino Calace, Gaia Bonnetti, Marco Gabaglio, Sabeya Cuganathan

Selected publications

Misra T, Baccino-Calace M, Meyenhofer F, Rodriguez-Crespo D, Akarsu H, ..., Frei C, Cantera R, Egger B & Luschig S (2016). A genetically encoded biosensor for visualizing hypoxia responses in vivo. *Biology Open* 6: 296-304

Guillermin O, Perruchoud B, Sprecher SG, and Egger, B. (2015) Characterization of tailless functions during *Drosophila* optic lobe formation. *Developmental Biology* 405, 202-213.

Southall T.D., Gold K.S., Egger B., Davidson C.M., Caygill E.E., Marshall O.J., and Brand A.H. (2013) Cell-type-specific profiling of gene expression and chromatin binding without cell isolation assaying RNA Pol II occupancy in neural stem cells. *Developmental Cell* 26, 101-112.



Since Tll/TLX transcription factors are evolutionary highly conserved between flies and mammals our findings are relevant to gain insights into neural stem cell state transitions during our own brain development.

(A) Neural stem cells undergo symmetric proliferative divisions to expand a progenitor pool. Subsequently, they switch either to asymmetric self-renewing division or differentiative symmetric divisions to generate more specialized cell types.

(B) shows a developing *Drosophila* brain, in which cells are labeled by immunofluorescent stainings.

(C) shows the corresponding graphical representation of the different progenitor types in the developing brain. Naïve neuroepithelial cells in darker green transform in more restricted lamina precursor cells labeled in lighter green and in asymmetrically dividing medulla neuroblasts in blue. The red neuroepithelial cells are in a transitory state from symmetrically dividing neuroepithelial cells to asymmetrically dividing neuroblasts.

What is the main task of the Bioinformatics Core Facility?



Dr Laurent Falquet

Bioinformatics

**Bioinformatics core facility of the
University of Fribourg**

At the Bioinformatics Unraveling Group of the University of Fribourg (BUGFri) we support life science researchers by providing expertise in data analysis of Next Generation Sequencing (NGS) experiments, or any large-scale biological experiment requiring bioinformatics resources. We focus on genome assembly, annotation and comparison as well as on mutant and structure variant identification by resequencing. We also perform metagenomics, RNAseq and ChIPseq data analysis, proteome clustering and ortholog/paralog classification, as well as pathway and gene set enrichment analysis.

We are part of a Sinergia project “Pangenomic and comprehensive analysis of the relationship between bacterial toxin-antitoxin systems and antibiotic phenotype”.

We developed PACMAN a web tool to visualize DNA methylation in Bacterial genomes.

<http://www.unifr.ch/bugfri/pacman>

Co-workers

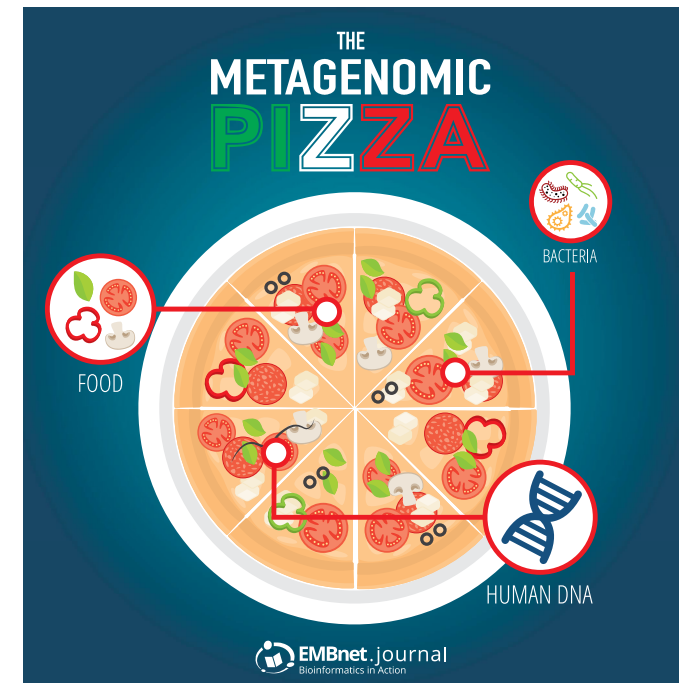
Dr Hatice Akarsu-Egger, Lisandra Aguilar-Bultet (UniBe)

Selected publications

Leake SL, Pagni M, Falquet L, Taroni F & Greub G (2016). The salivary microbiome for differentiating individuals: proof of principle. *Microbes and Infection* 18: 399-405.

Ritpitakphong U, Falquet L, Vimoltust A, Berger A, Métraux JP & L'Haridon F (2016). The microbiome of the leaf surface of *Arabidopsis* protects against a fungal pathogen. *New Phytologist* 210: 1033-1043.

Pillet B, García-Gómez JJ, Pausch P, Falquet L, Bange G, de la Cruz J & Kressler D (2015) The Dedicated Chaperone Acl4 Escorts Ribosomal Protein Rpl4 to Its Nuclear Pre-60S Assembly Site. *PLoS Genetics* 11: e1005565. doi:10.1371/journal.pgen.1005565





Dr Markus Geisler

Regulation of hormone transport complexes

Exploring the future without forgetting the past.

Our work aims at exploring the fascinating cell-to-cell movement of the plant signaling molecule, auxin. This event - called polar auxin transport - represents a unique, plant-specific mechanism that has puzzled mankind since its first description by Charles Darwin and now represents a hotspot in plant biology.

In the last years, we have been focusing mainly on the characterization of the individual transport proteins driving polar auxin transport. Moreover, using a combination of biochemical, in silico and imaging techniques, we were able to decipher their modes of regulation and their functional interactions with other transporters and regulatory components.

However, our special interest lies in the functional interaction between the ABC transporter, ABCB1, and TWISTED DWARF1. Recent work reveals that TWISTED DWARF1 acts as a chaperon during ABCB1 plasma membrane delivery in analogy to its human ortholog, CFTR. Defects in CFTR cause a frequent disease called cystic fibrosis or mucoviscidosis.

Co-workers

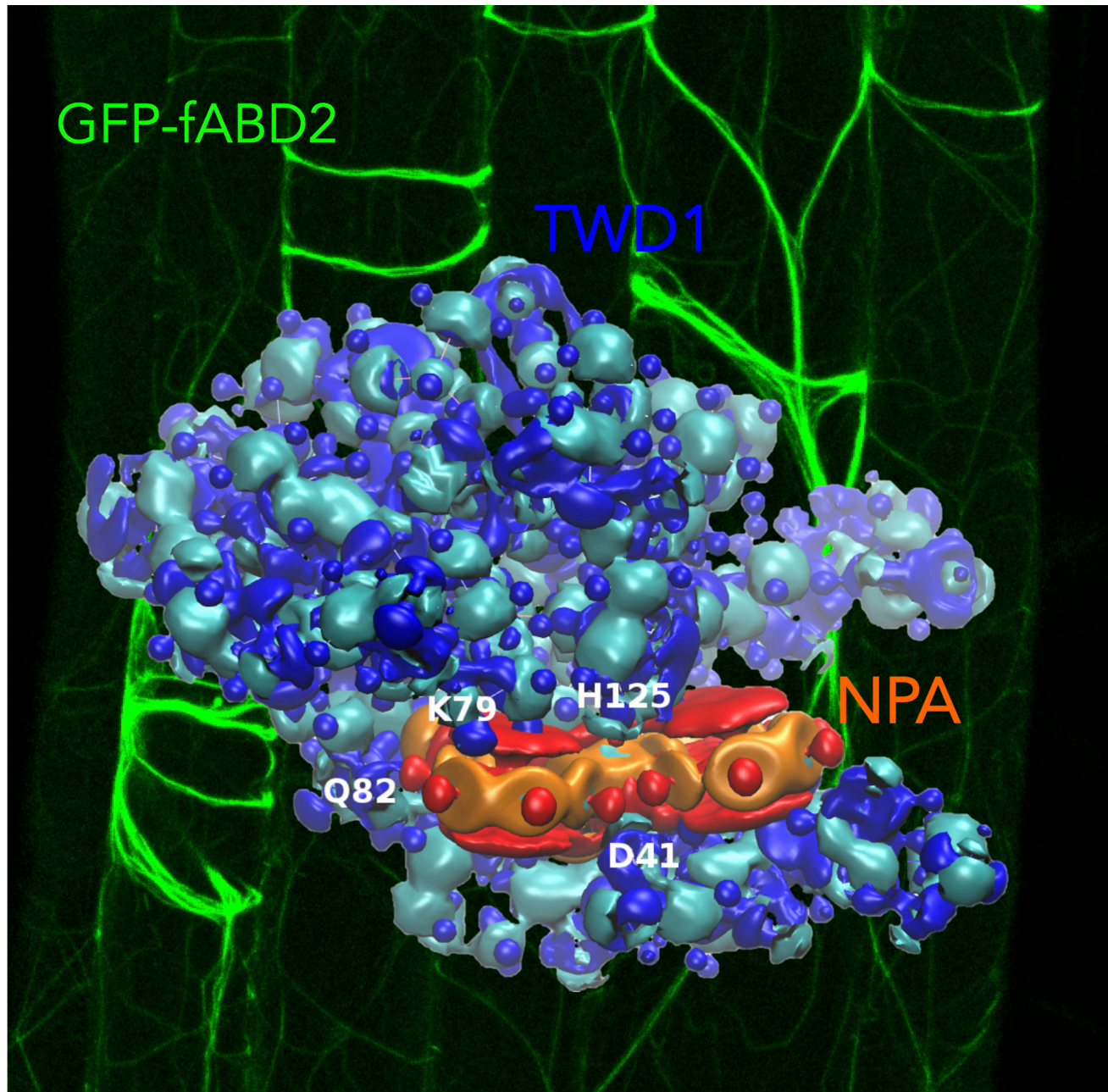
Bibek Aryal, Martin Di Donato, Pengchao Hao, John Huynh, Laurence Charrier

Selected publications

Aryal B, Laurent C and Geisler M (2016) Learning from each other: ABC transporter regulation by protein phosphorylation in plant and mammalian systems. *Biochem. Soc. Trans.* 4: 663-673

Zhu J et al. (2016) TWISTED DWARF1 mediates the action of auxin transport inhibitors on actin cytoskeleton dynamics. *The Plant Cell* 28: 930-48

Ivanchenko M et al. (2015) The cyclophilin-A DIAGEOTROPICA gene affects auxin transport in both root and shoot to control lateral root formation. *Development* 142: 712-721



TWISTED DWARF1 mediates NPA action on actin dynamics.

Both polar auxin transport and vesicle cycling are inhibited by synthetic auxin transport inhibitors, such as NPA. By using NMR and in silico docking, we mapped the NPA binding surface on the chaperone, TWISTED DWARF1 (TWD1), and identified ACTIN7 as a relevant TWD1 interactor.

The picture on the left shows increased cortical actin bundling (green fluorescence) upon NPA treatments visualized by the actin marker, GFP-fABD2. Quantum chemical analysis of the electron density components allowed identifying the contact region between NPA (orange) and TWD1 (blue).



Prof. Dominique Glauser

Molecular and cellular bases of nociception and its plasticity

A small worm teaching us how to shut off pain signals

Pain is a major patient concern in disease. Because available drugs are either only moderately effective or have detrimental side effects, there is an essential need for novel therapeutic solutions in pain management. Progresses in the field are hindered in human and mammalian models by the size and the complexity of the nervous system, as well as the difficulty to bridge the gaps in our understanding at the molecular, neuronal, and physiological/behavioral levels.

To circumvent these limitations, our lab uses the simple model organism *Caenorhabditis elegans* to identify new mechanisms controlling nociception (the detection and encoding of noxious stimuli in the nervous system) and delineate new potential drug targets. We have established a powerful pipeline enabling the identification and characterization of new genes required for nociception and avoidance behaviors. This approach involves a genome-scale mutagenesis screen creating mutants with decreased pain sensitivity. We use them as entry points to discover and characterize novel molecular pathways controlling nociception.

Co-workers

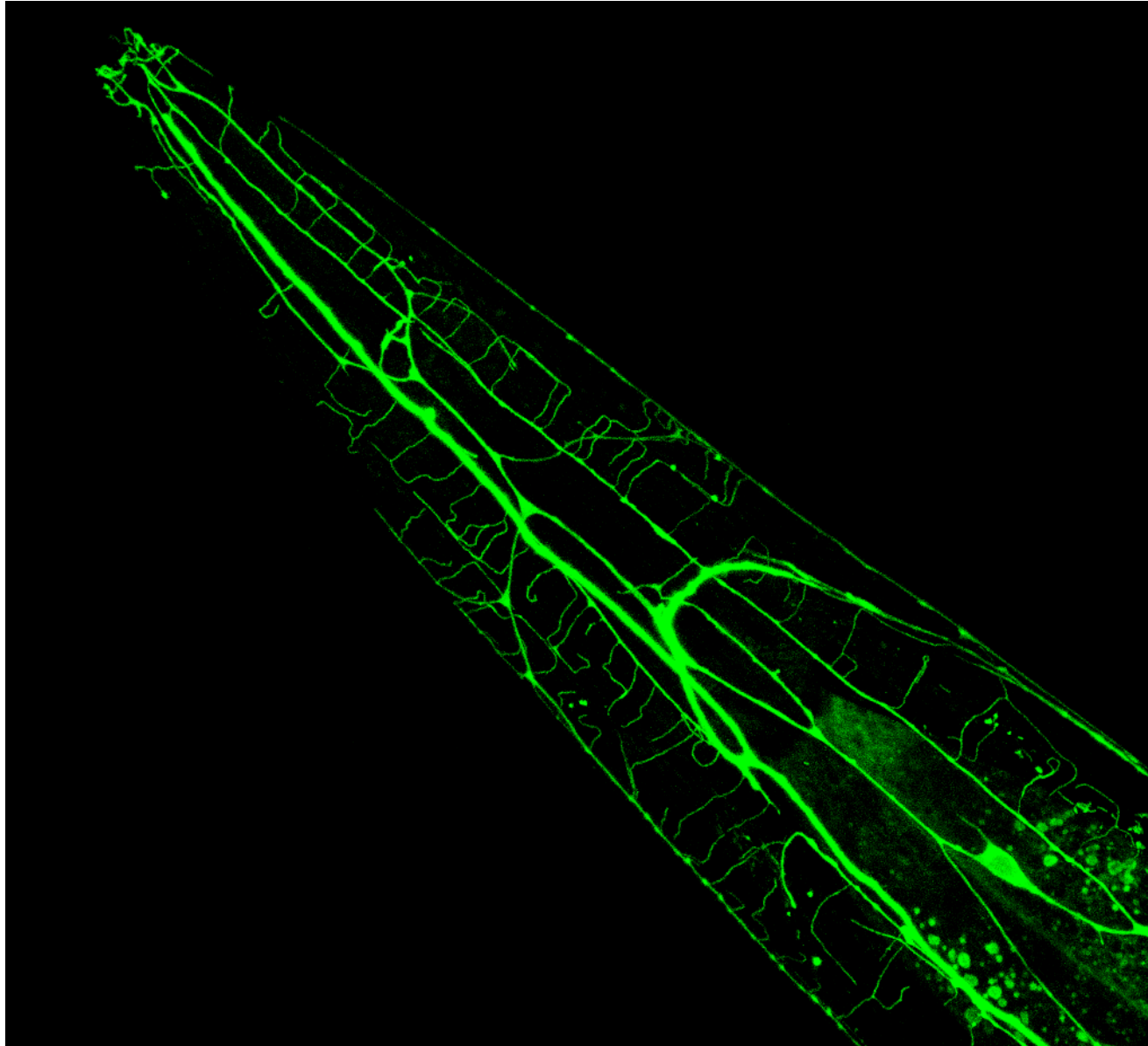
Riccardo Dore, Lola Hostettler, Domenica Ippolito, Vanina Lauper, Andrei Lia, Filipe Marques, Gabriella Saro, Lisa Schild, Laurie Zbinden

Selected publications

Glauser DA and Goodman MB (2016) Molecules empowering animals to sense and respond to temperature in changing environments. *Curr Opin Neurobiol.*41:92-98

Schild LC, Glauser DA (2015) Dual Color Neural Activation and Behavior Control with Chrimson and CoChR in *Caenorhabditis elegans*. *Genetics* 200(4):1029-1034

Schild LC, Zbinden L, Bell HW, Yu YV, Sengupta P, Goodman MB, Glauser DA (2014) The Balance between Cytoplasmic and Nuclear CaM Kinase-1 Signaling Controls the Operating Range of Noxious Heat Avoidance. *Neuron* 84(5):983-96



Nociceptor neuron imaged in a living transgenic *Caenorhabditis elegans* nematode

With its small size and a transparent body, *C. elegans* is an ideal model for *in vivo* imaging. We recently developed improved transgenic tools for *in vivo* cellular biology in *C. elegans*, such as mNeonGreen, a markedly brighter alternative to the classical green fluorescent protein (GFP). mNeonGreen superbly highlights the arborized morphology of this thermal nociceptor neuron in the head of *C. elegans*.

Picture taken at the Bioimage Facility by Lola Hostettler during her Master thesis work in the Glauser lab.



Prof. Claire Jacob

Epigenetic control of maintenance and regeneration in myelinating glia

Can we program de-/re-generation of the nervous system?

Our research aims at elucidating basic mechanisms of chromatin remodeling in the control of neuroprotection and neuroregeneration in the peripheral and central nervous systems (PNS and CNS, respectively) and testing our findings as exploratory treatments in animal models for potential cures. We study in particular traumatic lesions of the PNS and CNS, and degenerative diseases due to functional defects in myelinating cells (e.g. peripheral neuropathies and multiple sclerosis). Our research is focused on the functions of chromatin-remodeling enzymes, which control gene expression and have the high potential to reprogram cells. We combine a wide range of approaches including among others mouse genetics, electron microscopy, microfluidics, high-resolution live-cell imaging (4D), molecular and cellular biology, in-vitro and in-vivo gene delivery/silencing by viral vectors, mass spectrometry, RNA sequencing.

Co-workers

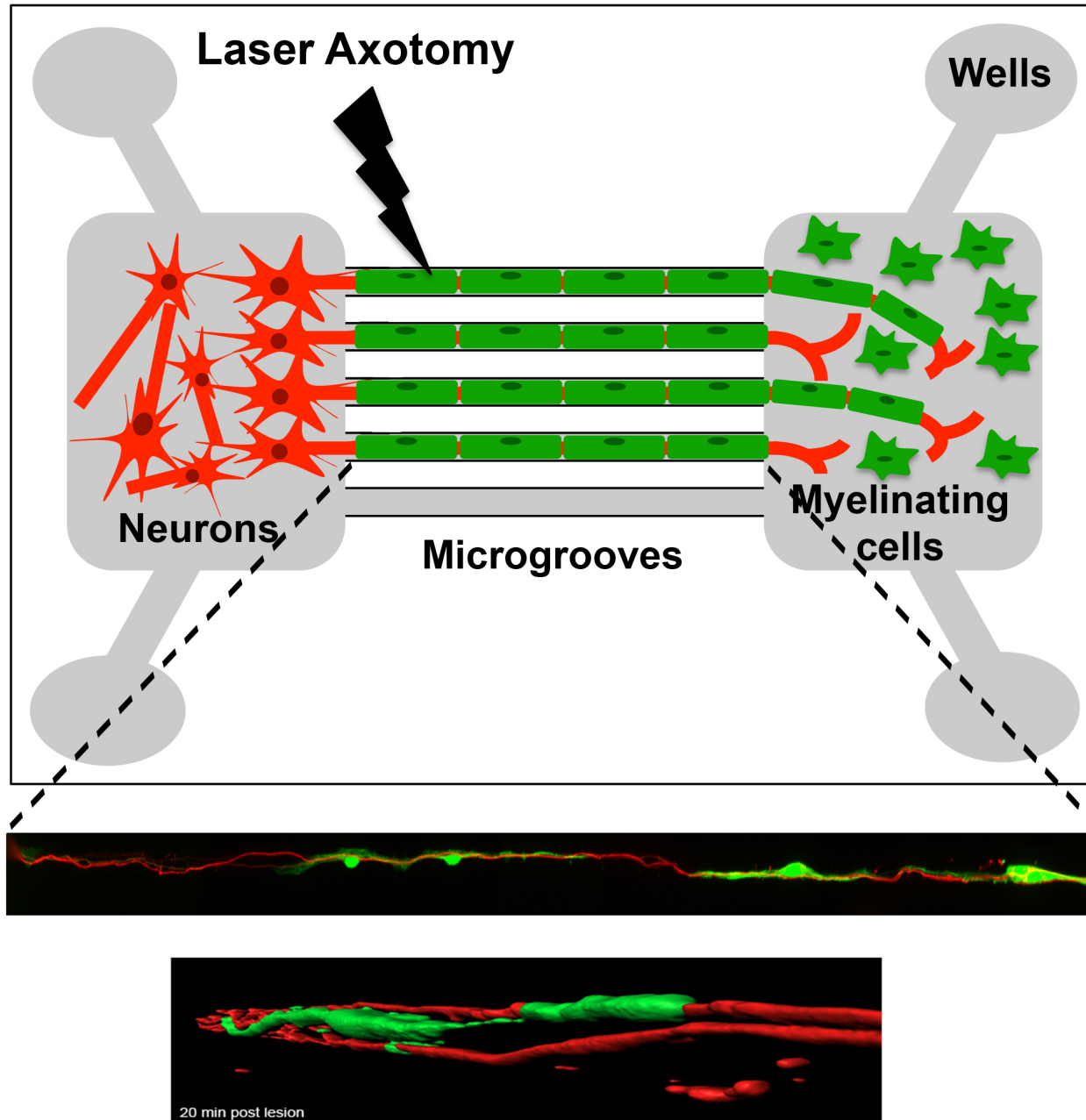
Valérie Brügger, Sophie Ruff, Adrien Vaquié, Mert Duman, Alizée Sauvain

Selected publications

Brügger V et al. (2017) Delaying histone deacetylase early response to injury accelerates conversion into repair Schwann cells and nerve regeneration. *Nat Comm* 10.1038

Brügger V et al. (2015) HDAC1/2-dependent PO expression maintains paranodal and nodal integrity independently of myelin stability through interactions with neurofascins. *PLOS Biol* 13(9): e1002258.

Jacob C et al. (2011) Schwann cell survival and myelination are critically dependent on HDAC1 and HDAC2 function. *Nat Neurosci* 14: 429-436



Our work demonstrates key chromatin remodeling functions in maintaining paranodes and nodes of Ranvier, two essential structures for neuronal activity. The mechanism we identified is critical for PNS integrity, its disruption leading to neurodegenerative diseases. We believe that these findings could be used to design new therapeutic strategies to prevent neurodegeneration.

Our second line of research identifies basic mechanisms of axonal regrowth and remyelination after traumatic lesions of the PNS and demonstrates in-vivo efficiency of novel treatments to accelerate regeneration and functional recovery after lesion. By using models of PNS and CNS lesions that we have set up in microfluidic chambers, we test these strategies to regenerate CNS lesions, and validate our findings in vivo.



Prof. Anna Jazwinska

Tracking the mystery of organ regeneration in zebrafish

How and why organs can or cannot regenerate after injury are important questions.

Humans are not able to regenerate their damaged heart and limbs, but certain vertebrates possess such capabilities. The zebrafish is the ideal model for investigation of regeneration, due to its power to restore complex organs and the existence of molecular genetic tools. Conceptual understanding of the natural mechanisms of regeneration will pave the way for novel medical strategies for treatment of injuries in people. In our laboratory, we are exploring the molecular and cellular triggers of heart and fin regeneration in zebrafish, and have made some intriguing discoveries.

Co-workers

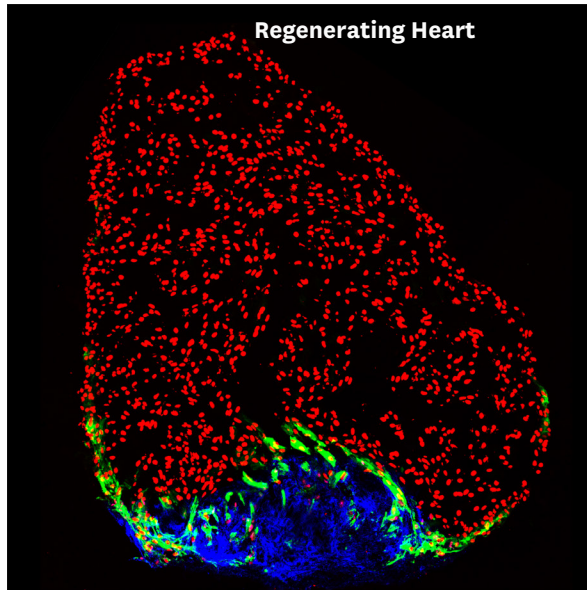
Verena Zimmermann, Catherine Pfefferli, Anne-Sophie de Preux Charles, Simon Blanchoud, Pauline Sallin, Bérénice Chassot, Désirée König, Thomas Bise, Jan Marro, David Pury

Selected publications

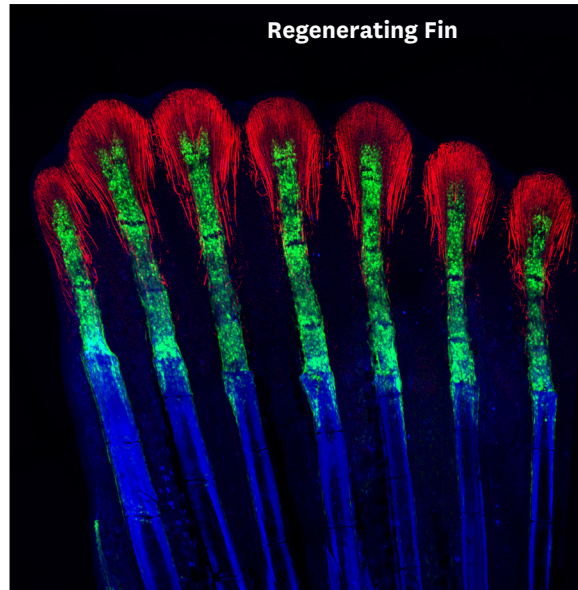
de Preux Charles A-S, Bise T, Baier F, Marro J, Jazwinska A. (2016) Distinct effects of inflammation on preconditioning and regeneration of the adult zebrafish heart. *OPEN BIOLOGY* (The Royal Society Publishing)

Chassot B, Pury D, Jazwinska A. (2016) Zebrafish fin regeneration after cryoinjury-induced tissue damage. *BIOL. OPEN* (The Company of Biologists) 5: 819-828

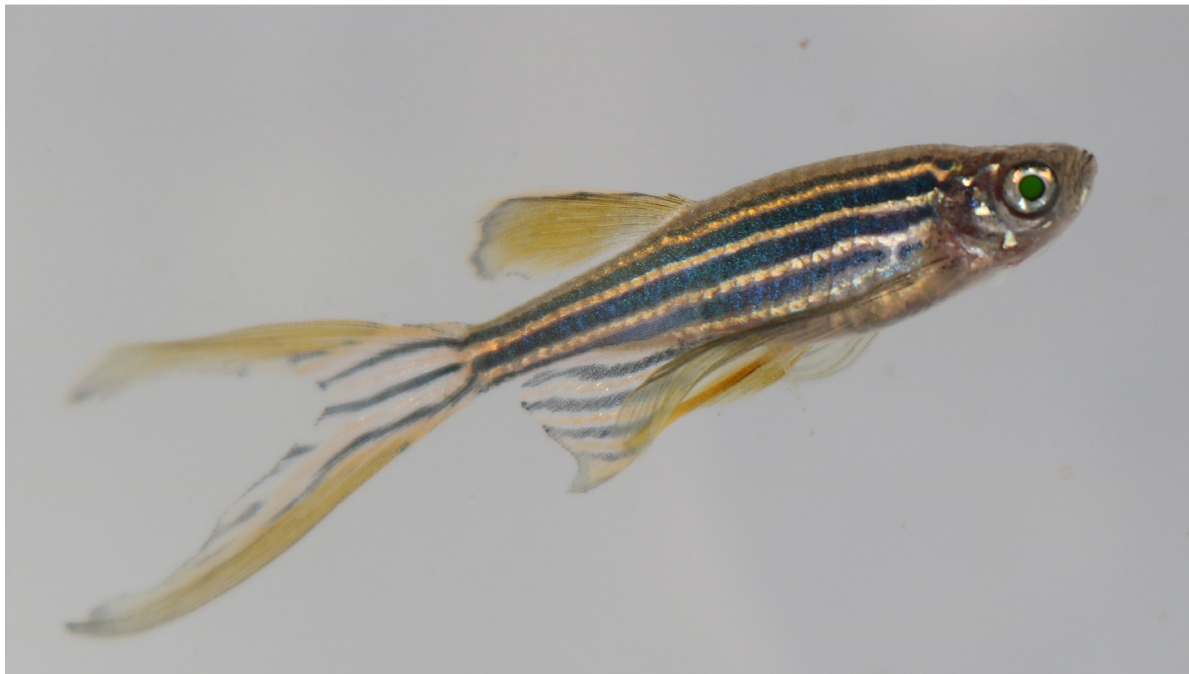
Jazwinska A., Sallin P. (2016) Regeneration versus scarring in vertebrate appendages and heart. *JOURNAL OF PATHOLOGY*; 238(2):233-46.



Regenerating Heart



Regenerating Fin



Heart regeneration

Several years ago, our laboratory has established a cryoinjury procedure in the adult zebrafish heart, which mimics physiologic responses of mammalian myocardial infarction, such as massive cell death, inflammation and fibrotic tissue deposition. We have shown that a damage of 20% of the ventricle can be replaced by new myocardium within 30 to 60 days. Our laboratory has also demonstrated that this robust regenerative process is regulated by both paracrine signals, such as TGF- β signaling, as well as systemic endocrine factors, such as stress hormones. We uncovered that adult zebrafish display tremendous plasticity to respond to injury signals through partial de-differentiation and proliferation of functional cells. Knowledge of the mechanisms of heart regeneration in zebrafish could, in the long term, be translated into new treatments for human heart attack patients.

Conservation of species, a key issue for our future.



Prof. Gregor Kozlowski

Conservation biology
and biogeography

The research in our group focusses on conservation biology and biogeography of relict, endemic and threatened organisms. Our main study and model taxa are woody plants with disjunct distribution pattern, with main interest on the genus *Zelkova* (Ulmaceae) and *Pterocarya* (Juglandaceae). Additional interest touches the evolutionary processes, biogeographical patterns and conservation issues of aquatic, coastal and alpine plants, both at regional and global scale. We are using various biogeographical, molecular and dendrochronological methods and are conducting an intensive field work in the Alps and adjacent mountain chains, in the Mediterranean (e.g., Crete, Sicily), in Transcaucasia (e.g., Georgia, Azerbaijan) and in Eastern Asia (e.g., China, Japan, Vietnam).

Our group is part of the Botanic Garden of the University of Fribourg (G. Kozlowski is a curator of the garden) and is intensively collaborating with the Natural History Museum Fribourg (NHMF).

More information under www.zelkova.ch.

Co-workers

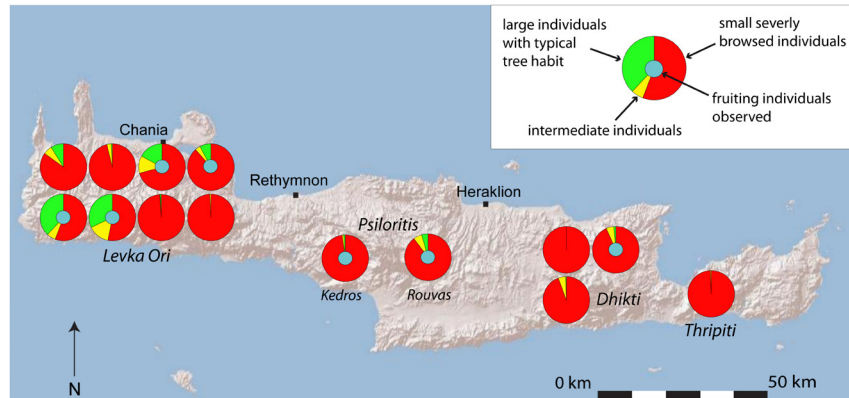
Sébastien Bétrisey, Marie Carron, Benoît Clément, Daniel Ducry, Laurence Fazan, Yann Fragnière, Eveline Kozlowski, Yi-Gang Song

Selected publications

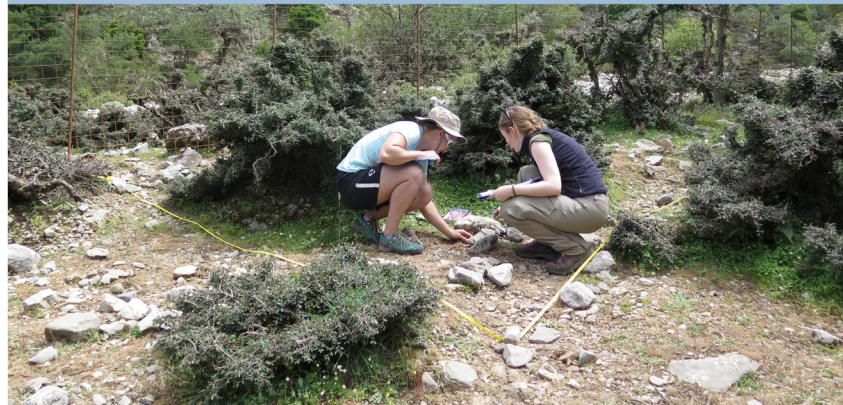
Arrigo N, Bétrisey S, L. Graf, J. Bilat, E. Gerber, G. Kozlowski. (2016) Hybridization as a threat in climate relict *Nuphar pumila* (Nymphaeaceae). *Biodiversity and Conservation* 25: 1863-1877

Fragnière Y, Bétrisey S, Cardinaux L, Kozlowski G. (2015) Fighting their last stand? A global analysis of the distribution and conservation status of gymnosperms. *Journal of Biogeography* 42: 809-820

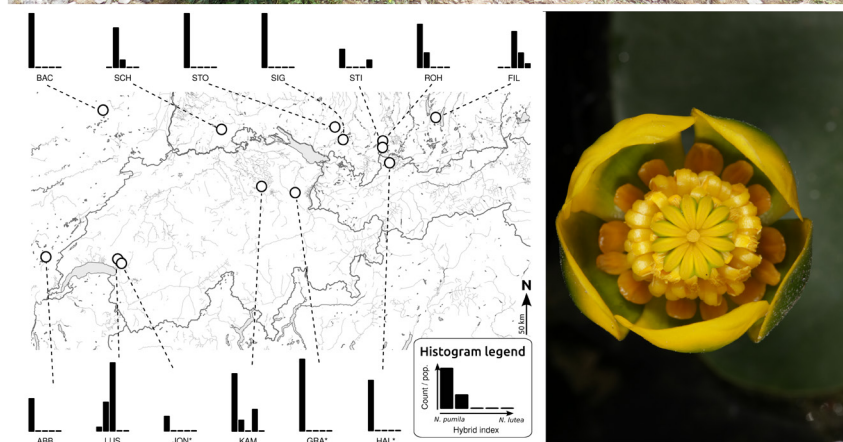
Christe C, Kozlowski G, Frey D, Bétrisey S, Maharramova E, Garfi G, Pirintsos S, Naciri Y. (2014) Footprints of past intensive diversification and structuring for the genus *Zelkova* (Ulmaceae) in southwest Eurasia. *Journal of Biogeography* 41: 1081-1093



Asymmetric population structure: The populations of *Z. abelicea* on Crete are totally dominated by dwarfed and heavily grazed individuals (Kozłowski et al. 2014)



Relict trees in peril: Monitoring of *Zelkova abelicea* (Ulmaceae) study plots on Crete. An intensive and exciting field work is a trademark of our scientific group.



(left) **Hybridization as a threat in climate relicts:** Our recent molecular study demonstrates an extremely high level of the admixture between *Nuphar pumila* (alpine and rare climate relict) and closely related and common lowland species *N. lutea* (Arrigo et al. 2016)



(right) **Climate relicts in the Alps:** *Nuphar pumila* (Nymphaeaceae) is one of the rarest aquatic plants in the Alpine Arc possessing only four extant populations in Switzerland.



Dr Dieter Kressler

**Analysis of eukaryotic
ribosome biogenesis in the yeast
*Saccharomyces cerevisiae***

Hold on to your friends - dedicated chaperones of ribosomal proteins

Ribosomes are the molecular machines devoted to the synthesis of all cellular proteins. Eukaryotic ribosomes are assembled from their components, the ribosomal RNA and ribosomal proteins (r-proteins), in a complex process, which takes primarily place in the nucleolus. An exponentially growing yeast cell produces more than 160'000 r-proteins per minute, and most of these r-proteins have to travel from the cytoplasm to their incorporation site on pre-ribosomes within the nucleus. Due to their difficult physicochemical properties, r-proteins are especially prone to aggregation and, hence, the synthesis of assembly-competent r-proteins represents a major challenge. Recent evidence has revealed that r-proteins, besides relying on the general chaperone and transport systems, may also employ specialized binding partners, termed dedicated chaperones, in order to ensure their soluble expression, nuclear import and/or correct assembly into pre-ribosomes.

Our recent work has defined a novel step of ribosome biogenesis, beginning as early as with the co-translational recruitment of dedicated chaperones to nascent r-proteins. Moreover, we have identified a novel dedicated chaperone and revealed how sequential domain assembly of an r-protein drives pre-40S maturation.

Co-workers

Dr Guillaume Murat, Benjamin Pillet and Ujjwala Singh.

Collaborations:

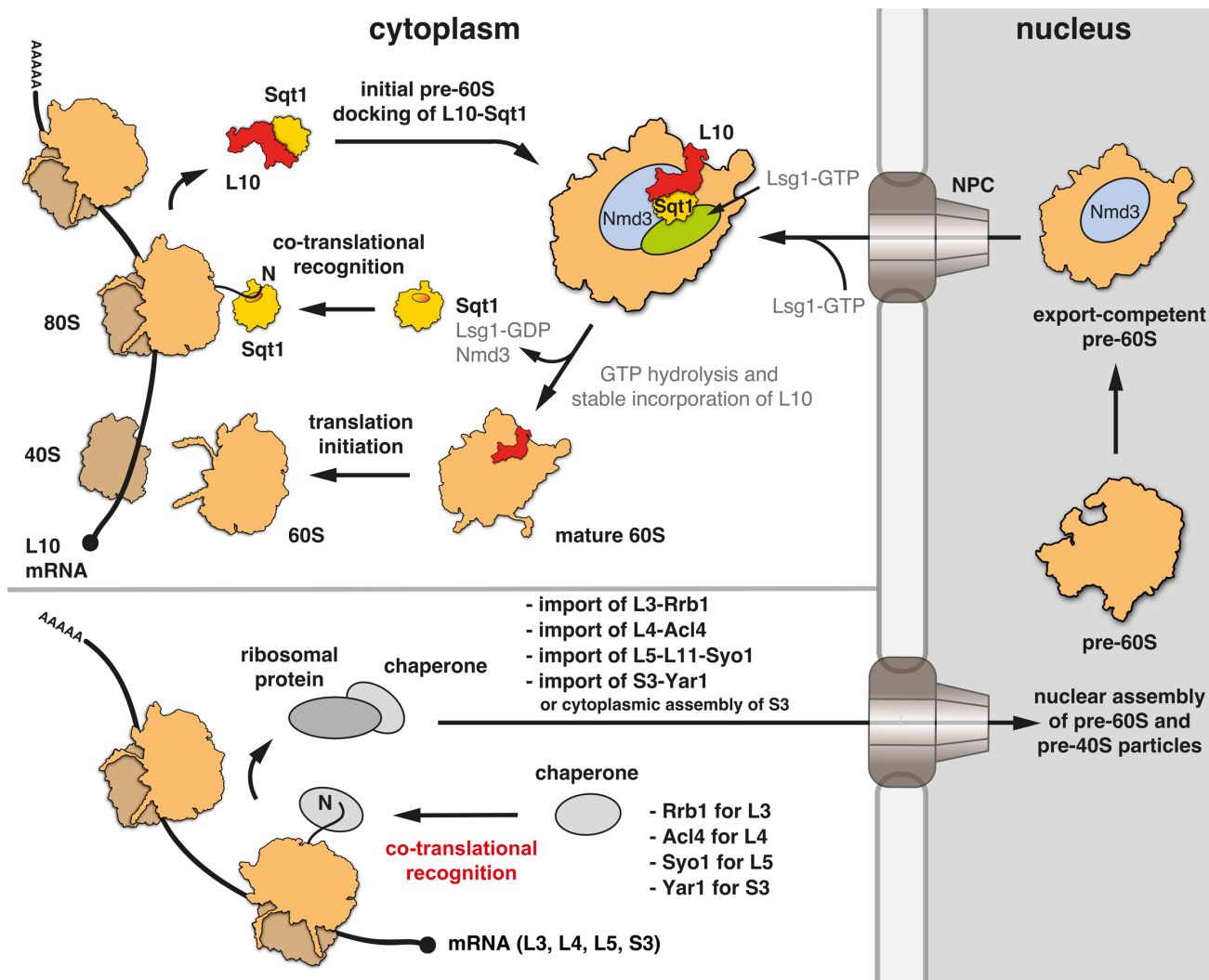
Dr. Gert Bange (Universität Marburg), Pr. Jesús de la Cruz (Universidad de Sevilla), Pr. Nicolas Leulliot (Université Paris Descartes), and Dr. Brigitte Pertschy (Universität Graz).

Selected publications

Pausch P et al. (2015) Co-translational capturing of nascent ribosomal proteins by their dedicated chaperones. *Nat Commun* 6:7494.

Pillet B et al. (2015) The dedicated chaperone Acl4 escorts ribosomal protein Rpl4 to its nuclear pre-60S assembly site. *PLoS Genetics* 11:e1005565.

Mitterer V et al. (2016) Sequential domain assembly of ribosomal protein S3 drives 40S subunit maturation. *Nat Commun* 7:10336.



Co-translational capturing of r-proteins by their dedicated chaperones.

Upper left part: Sqt1 recognizes the N-terminal residues of L10 as these emerge from translating ribosomes. Initial docking of Sqt1-bound L10 onto Lsg1-defined pre-60S subunits involves L10 surfaces that are not shielded by Sqt1 and pre-60S sites that are not masked by Nmd3. The GTPase Lsg1 promotes structural rearrangements that entail release of Nmd3 and stable incorporation of L10, leading to the formation of mature 60S subunits. Lower left part: The dedicated chaperones Acl4, Rrb1, Syo1, and Yar1 also capture their r-protein clients L4, L3, L5, and S3 in a co-translational manner. Right part: Pre-60S subunits gain export competence upon recruitment of Nmd3 and travel across the nuclear pore complex (NPC) to the cytoplasm.



Prof. Felix Mauch

Plant immunity

Molecular warfare between plants and the oomycete pathogen *Phytophthora*

Just like any living organism plants can fall victim to microbial pathogens and were forced to evolve defense strategies in order to survive. The immune system of plants is remarkable similar to the innate immune system of animals. It consists of a number of immune receptors that can recognize diverse pathogen derived molecules and as a result will trigger a multitude of immune reactions. The efficacy of the plant immune system forced pathogens to evolve counter strategies in form of effectors that are delivered into host cells with the aim to sabotage plant immune responses. My group is interested in the interaction of plants with the oomycete pathogen genus *Phytophthora* that includes the notorious potato pathogen *P. infestans* that caused the great Irish potato famine and is still a threat to agricultural production. We have established a model pathosystem with *Arabidopsis* as the host and *P. brassicae* as pathogen that allows us to analyze both sides of the interaction at the molecular level. One of the main questions we ask is: Which plant immune reactions are important for defense against *Phytophthora*? Currently we work on the PATHOGENESIS-RELATED PROTEIN 1 (PR-1) that has been discovered 50 years ago as one of the first pathogen-induced proteins but whose biochemical function has remained elusive.

We recently showed that PR-1 inhibits microbial growth via its sterol-binding activity. PR-1 is especially effective in inhibiting sterol-auxotroph pathogens such as *Phytophthora*. The second question we address is: How does *Phytophthora* undermine specific plant immune reactions? To this end we aim to determine the molecular targets of *Phytophthora* effector proteins. The identified targets include proteins involved in the secretory process and in the functioning of plasmodesmata..

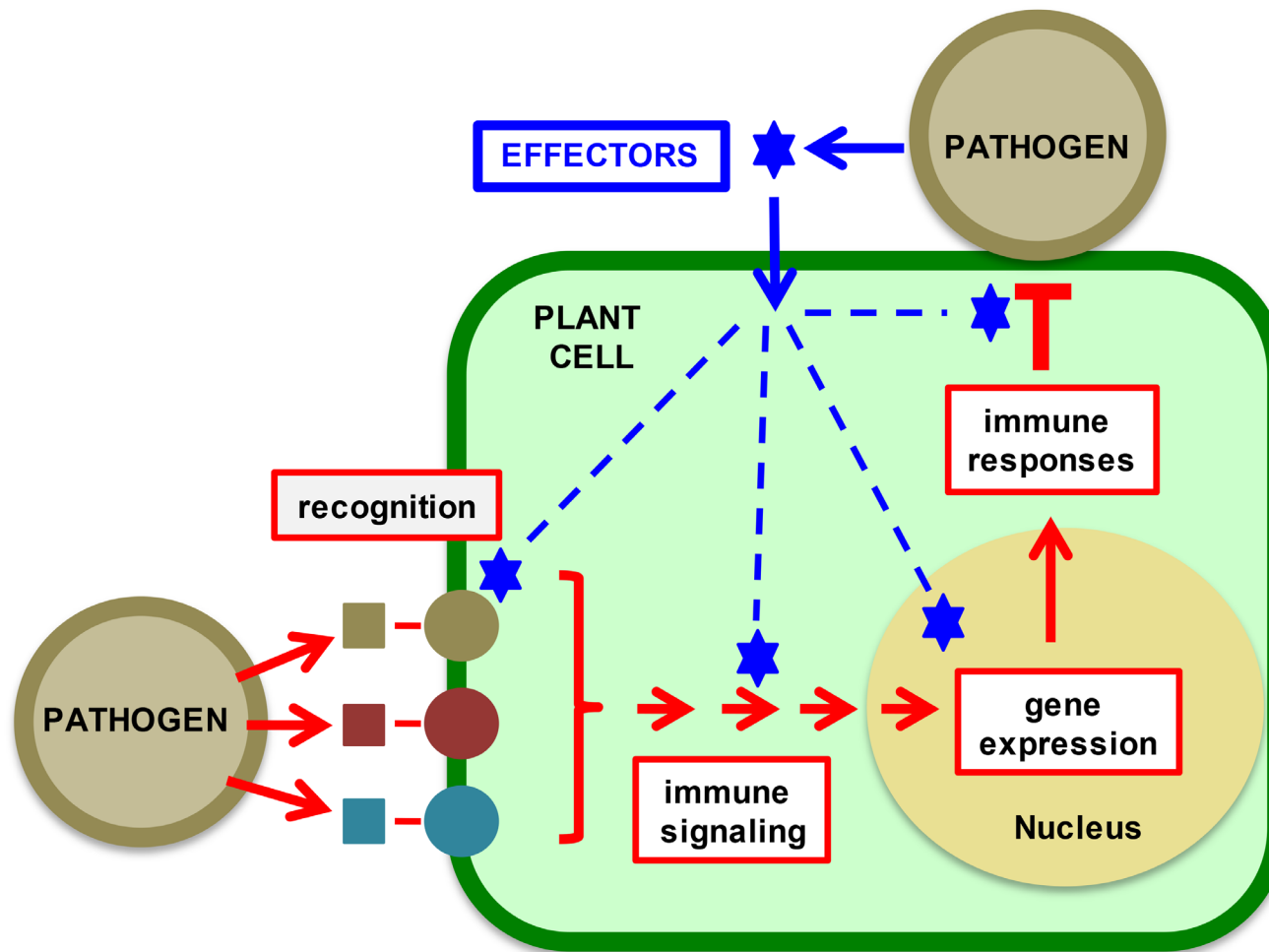
Co-workers

Dr Michael Stumpe, Dr Jordi Gamir, Iga Tomczynska, Aboubakr Moradi, Brahim Oubaha, Tu Giang Doan, Fanny Louviot, Katia Zbinden

Selected publications

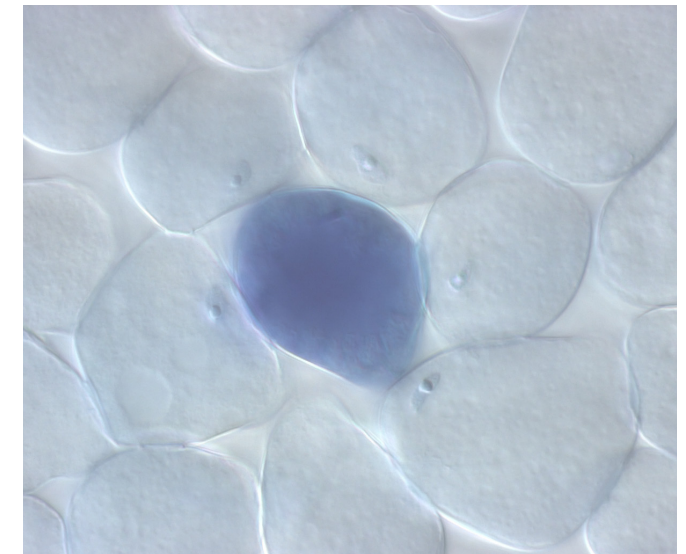
Gamir *et al.* (2016) The sterol-binding activity of PATHOGENESIS-RELATED PROTEIN 1 reveals the mode of action of an antimicrobial protein. *Plant Journal*, 62, 840-851.

Schlaeppli *et al.* (2010) Disease resistance of *Arabidopsis* to *Phytophthora brassicae* is established by the sequential action of indole glucosinolates and camalexin. *Plant Journal* 62, 840-851.



Plant defense reactions including pathogen recognition, defense signaling and individual immunity responses are targeted by pathogen-derived effector proteins that act as virulence factors to promote pathogen growth.

A typical plant defense reaction is the hypersensitive response at the site of pathogen penetration (blue cell). It is a cellular suicide reaction (apoptosis) that prevents the establishment of biotrophic pathogens. Interestingly, nuclei from neighboring cells move toward the dying cell.



(Top) The basics of plant immunity.

(Right) Cellular suicide reaction (blue) in response to pathogens with attracted nuclei from cells.



Dr Laurent Mène-Safrané

Plant nutrigenomics

Understanding and improving vitamin E biosynthesis in human diet.

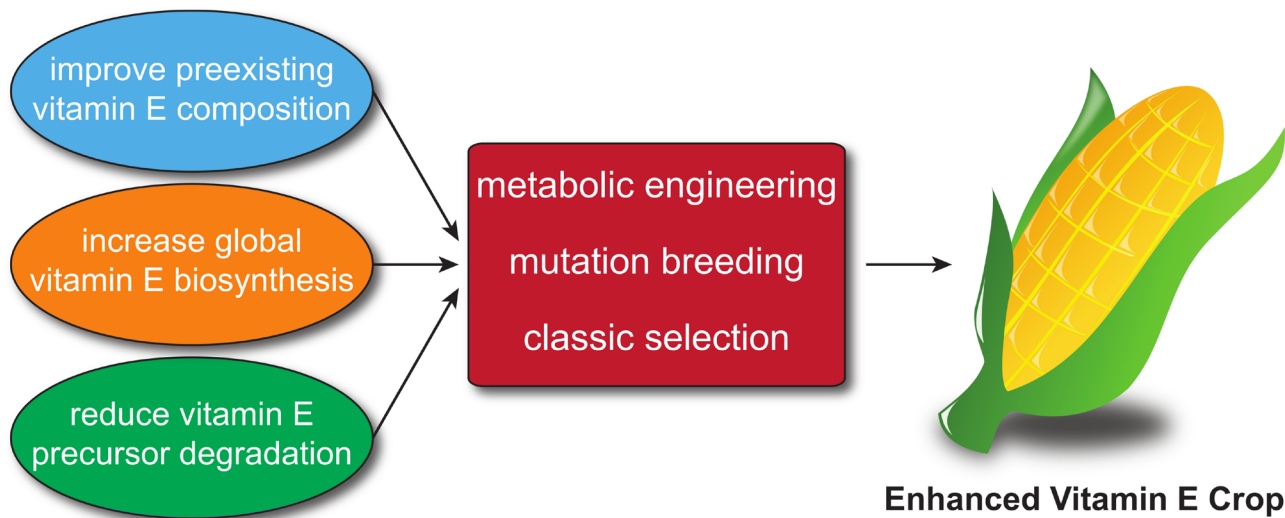
Improving vitamin E content in human diet. Vitamin E encompasses eight organic compounds (4 tocopherols and 4 tocotrienols) that are essential for human health. Recent nutritional surveys have shown that a significant proportion of the human population does not consume enough vitamin E and is consequently deficient for this vitamin. Such inadequacy is notably associated to increased risks of miscarriage in women pregnancy. In order to improve the vitamin E content in human diet (Figure 1, Top), my group is currently investigating the regulation of its biosynthesis in plants. The aim of our research is to identify the genes and the molecular mechanisms underlying the synthesis of this essential nutrient.

Co-workers

Sébastien Pellaud, Sébastien Bruisson, Alexandre Bory, Joëlle Romanens

Selected publication

Mène-Safrané, L. & Pellaud, S. Current strategies for vitamin E biofortification of crops. *Curr Opin Biotechnol* doi:10.1016/j.copbio.2017.01.007 (2017).



Scientific approaches and results.

To identify the molecular mechanisms regulating both vitamin E quantity and composition (Figure 1, Bottom-left), we developed a novel approach designated Next-Generation Nutrigenomics based on high-throughput analytics and whole-genome sequencing. This methodology allowed us to confirm 26 vitamin E mutants covering different aspects of the regulation of vitamin E biosynthesis. For instance, we identified several mutants that accumulate twice as much vitamin E than control plants (Figure 1 Bottom-right). We are currently characterizing these mutants in order to delineate which mechanisms control vitamin E synthesis in plant seeds.

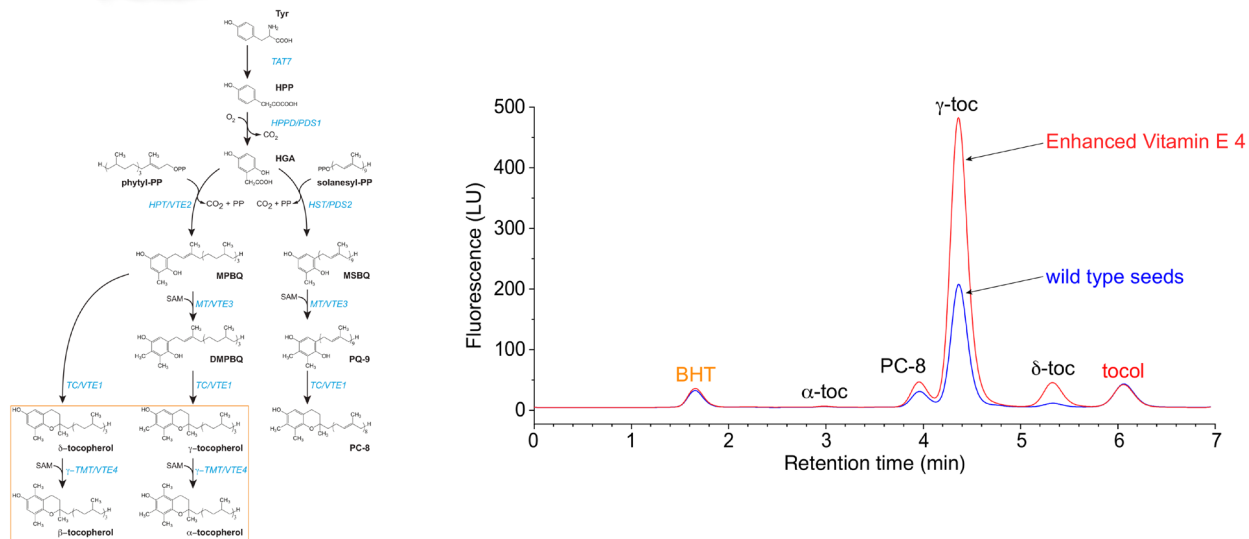


Figure 1 (Top) Current strategies used to improve vitamin E content in plants (Bottom-left) Vitamin E biosynthetic pathway in the oilseed model *Arabidopsis*. (Bottom-right): Identification of the Enhanced Vitamin E mutant.



Prof. Heinz Müller-Schärer

Ecology and evolution of plant
antagonist interactions

Biological Invasions: causes, consequences and management options

Besides their great relevance for the environment, biological invasions have been recognized as unprecedented bio-geographical experiments to study fundamental ecological and evolutionary processes, such as e.g. local adaptation to the novel conditions in the introduced range.

Like no other plant, *Ambrosia artemisiifolia*, common ragweed, has raised the awareness of invasive plants in Europe, causing great damage to our society due to its highly allergenic pollen, and as an important and hard-to-control crop weed. The recently and accidentally introduced leaf beetle *Ophraella communa* has the potential to reduce the population density and pollen production of ragweed in Europe.

We set out to analyze both potential benefits and risks of this biological control candidate by combining experimental studies under controlled conditions and in the field, with demographic and species distribution modeling and with genomics in view of predicting outcomes of this plant-insect interaction in various ecological settings as well as in the future (Figure 1, Top).

Co-workers

Prof. Urs Schaffner, Prof. Asad Shabbir, Prof. Yongjian Wang, Dr Suzanne Lommen, Dr Sarah Bouchemousse, Dr Yan Sun, Maria Litto, Benno Augustinus, Joelle Romenens, Nilgün Sailer.

Selected publications

Stutz S, et al. (2016) Ploidy level in the genus *Leucanthemum* correlates with resistance to a specialist herbivore. *Ecosphere*, 7(9) e01460.

Rosche Ch, et al. (2016). The population genetics of the fundamental cytotype-shift in invasive *Centaurea stoebe* s.l.: genetic diversity, genetic differentiation and small-scale genetic structure differ between cytotypes but not between ranges. *Biological Invasions*, 18: 1895-1910.

Sun Y, Müller-Schärer H, Maron JM, Schaffner U. (2015) Origin matters: diversity affects the performance of alien invasive species but not of native species. *The American Naturalist*, 185:725-736.

Areas of high conservation value at risk by plant invaders in Georgia under climate change

Situated between the Caucasus mountain ranges, Georgia is known for its high plant biodiversity and endemism, with up to 2'700 plant species endemic to the Caucasus region, 278 of them being strictly endemic to Georgia. This biodiversity hotspot is now increasingly threatened by invasive alien plants (IAP), often introduced in the context of pipeline constructions and land use change. In a survey and modeling study, we identified areas of high conservation value (AHCV) most at risk to 27 IAP, for which we assessed present and future potential distribution by using species distribution models (SDMs) under four climate change scenarios. We found IAPs presently to be mainly at low elevation, but that future climate change will allow IAPs to invade higher elevation sites, where more AHCV are found. Furthermore, we show that the actual Protected Areas cover only 9.4% of the areas of high plant endemism in Georgia (Figure 1, Bottom).

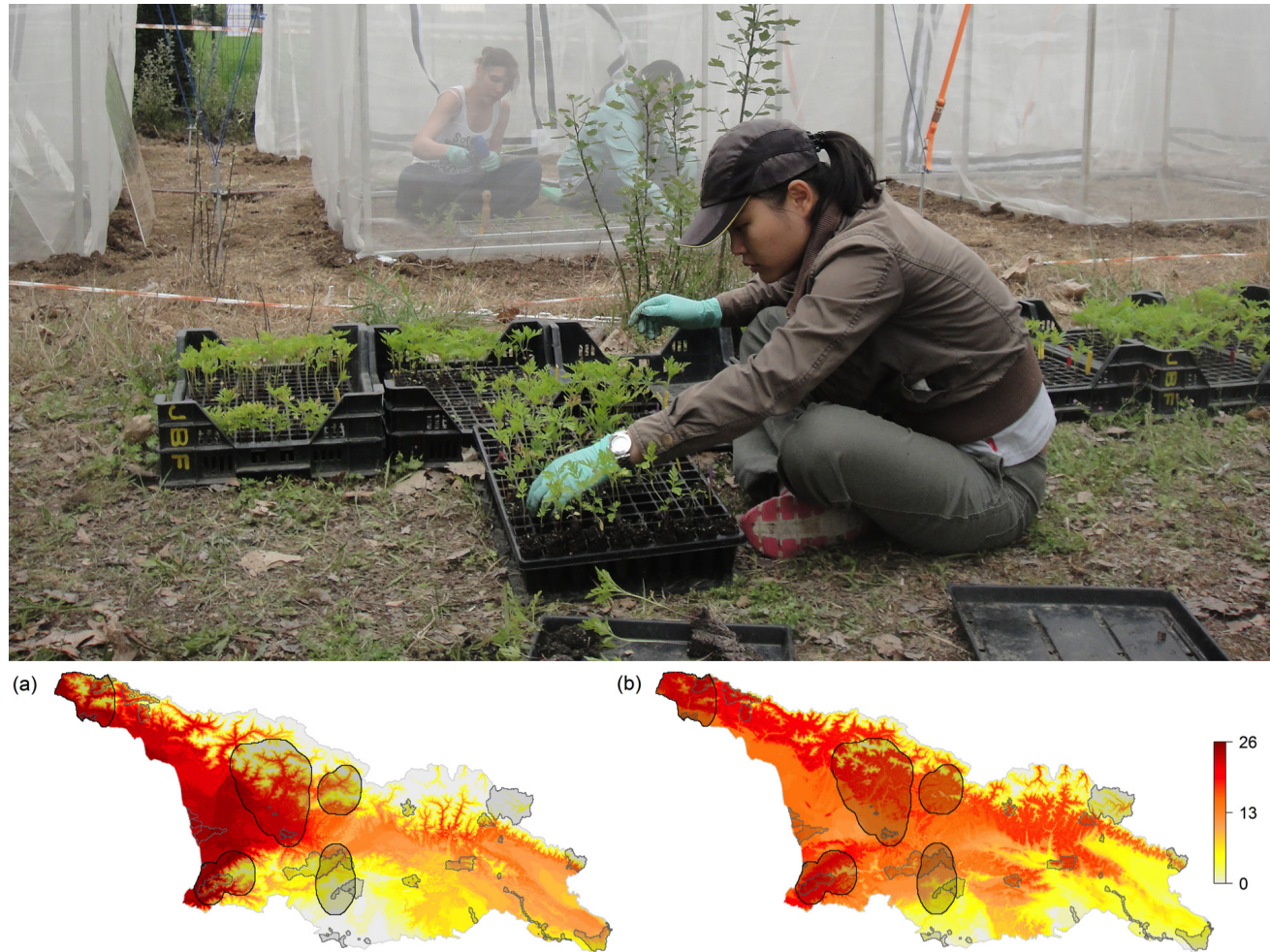


Figure 1 (Top) Setting-up a long-term selection experiment in Northern Italy to assess demographic and evolutionary changes in artificial *Ambrosia artemisiifolia* populations to warming (climate change) and insect herbivory by the leaf beetle *Ophraella communa*.

(Bottom) Invasive alien plant species richness in Georgia for the (a) present climate and (b) future climate for the year 2050 (RCP 8.5 IPSL-CM5A-LR climate change scenario). Each pixel represents the invasive alien plant richness on this site location (resolution: 1 km²). The protected areas are shown as grey-shaded frames and areas of high plant endemism as black-rimmed frames.

How do germ cells choose their destiny ?



Dr Alessandro Puoti

mRNA splicing and post-transcriptional regulation

In the hermaphroditic nematode *Caenorhabditis elegans*, primordial germ cells can develop either as spermatids or as oocytes. The question is how this decision is made at the molecular level. Of central interest in our laboratory is the *fem-3* mRNA, which is needed for the transient production of spermatids in the otherwise female somatic body of the hermaphrodite. *fem-3* mRNA is regulated post-transcriptionally through a distinct sequence in its 3'untranslated region. This regulatory element is recognized by specific proteins, which either directly bind to it or act through an unknown mechanism that involves the *mog* genes. We are currently exploring different possibilities, including splicing and regulation of mRNA stability. We use molecular genetic tools and microscopy.

Because post-transcriptional regulation of mRNAs exists in all eukaryotes, the nematode serves as a paradigm to understand the molecular mechanisms behind this process.

Co-workers

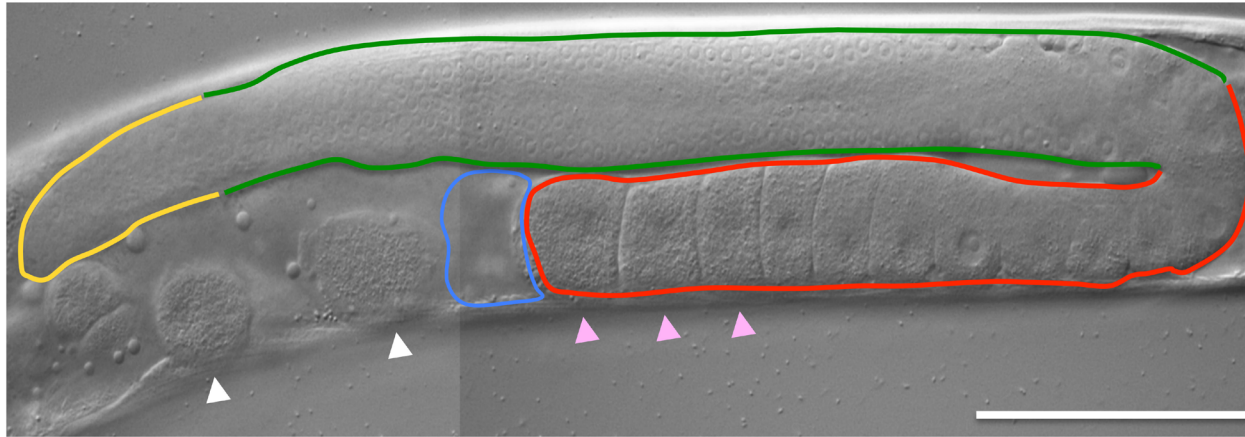
Maria Tarca, Roxane Dervey, Martine Ferry, Monica Couto, Christine Déforel

Selected publications

Zanetti S & Puoti A (2013). Sex determination in the *Caenorhabditis elegans* germline. *Advances in Experimental Medicine and Biology* 757: 41-69.

Zanetti S, Grinschgl S, Meola M, Belfiore M, Rey S, Bianchi P & Puoti A (2012). The sperm/oocyte switch in the *C. elegans* hermaphrodite is controlled through steady-state levels of the *fem-3* mRNA. *RNA* 18:1385-1394.

Zanetti S, Meola M, Bochud A & Puoti A (2011). Role of the *C. elegans* protein MOG-2 in sex determination. meiosis, and splice site selection. *Dev. Biol.* 354: 232-241.

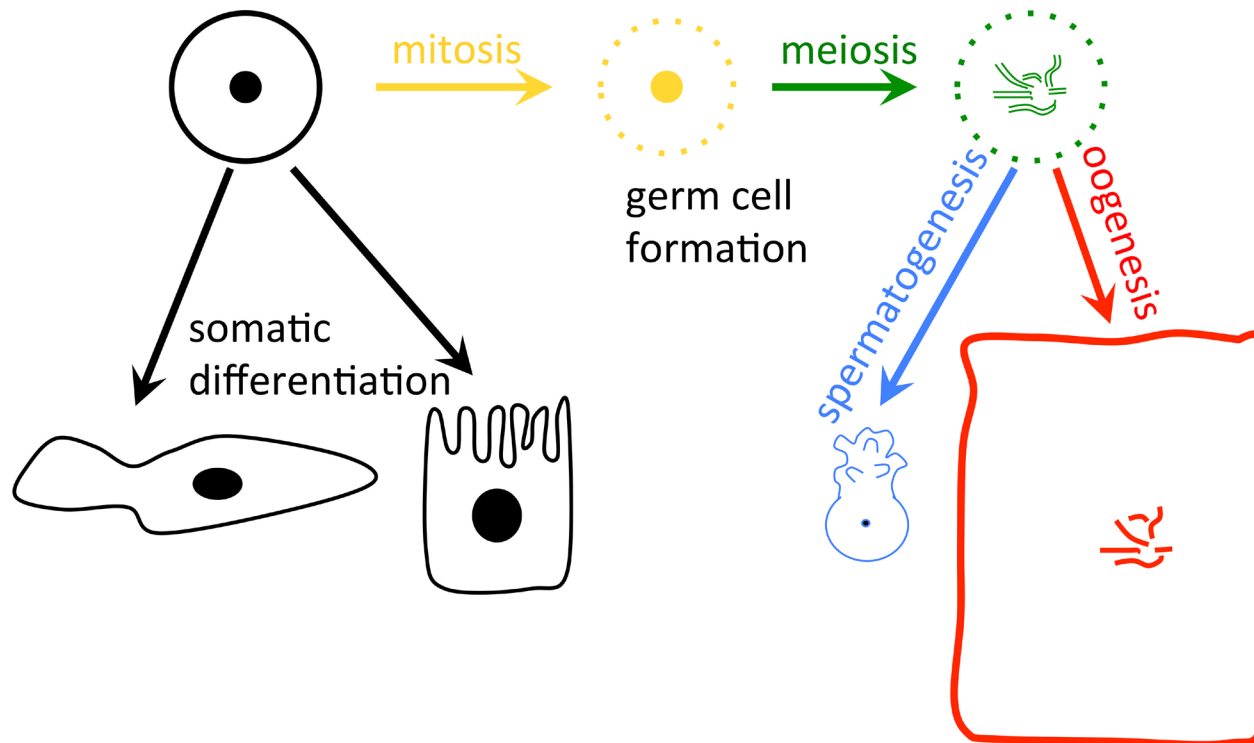


Cell fate decisions in the hermaphrodite germ line

One gonadal arm of an adult hermaphrodite germline is shown under differential interference contrast microscopy (scale bar, 50 μm). This organ allows to observe *in vivo* how germ cells form throughout a distal-proximal axis showing mitosis (yellow), followed by prophase I of meiosis (green) and more proximally oogenesis (red, with maturing oocytes indicated by pink arrowheads) and previously formed spermatids (blue). Fertilized eggs are found in the uterus (white arrowheads).

A precursor cell can differentiate in many ways: it can either be specified as a somatic or as a germ cell. Primordial germ cells (yellow) proliferate and eventually enter meiosis (green) to mature into sperm (blue) or oocytes (red).

We study the molecular mechanisms that control germ cell specification and differentiation.





Prof. Didier Reinhardt

Plant symbioses

How plants and beneficial fungi live in perfect harmony

Most plants live in symbiosis with microbes that improve their nutrition and play a central role in plant fitness in natural ecosystems. We study the arbuscular mycorrhizal (AM) symbiosis with fungi, that deliver phosphate to their host in exchange for carbohydrates. Two major questions are at the center of our work: 1.) How do the symbiotic partners find each other and communicate? and 2.) How is the symbiotic machinery established? We use genetic tools to identify genes required for AM symbiosis and to understand their function in the symbiosis. Using these tools we have identified the VAPYRIN protein which is required for the establishment of the fungal feeding structures (arbuscules) over which nutrients are exchanged. More recently, we have isolated a transcription factor which regulates many of the genes required for AM.

Co-workers

Pierre-Emmanuel Courty, Laure Bapaume, Eva Nouri, Mélanie K. Rich, Evert van Schaik, Flavien Buron, Martine Schorderet, Cris Kuhlemeier, Martin Frenz, Dominik Marti, Yamini Deb

Selected publications

M. K. Rich, M. Schorderet and D. Reinhardt (2014). The role of the cell wall compartment in symbiotic interactions of plants. *Frontiers in Plant Science* 5, 238.

M. K. Rich, M. Schorderet, L. Bapaume, L. Falquet, P. Morel, M. Vandenbussche, D. Reinhardt. (2015). The Petunia GRAS transcription factor ATA/RAM1 regulates symbiotic gene expression and fungal morphogenesis in arbuscular mycorrhiza. *Plant Phys.* 168, 788-797.

E. Nouri and D. Reinhardt (2015). Flowers and mycorrhizal roots - closer than we think? *Trends in Plant Science* 20, 344-350.

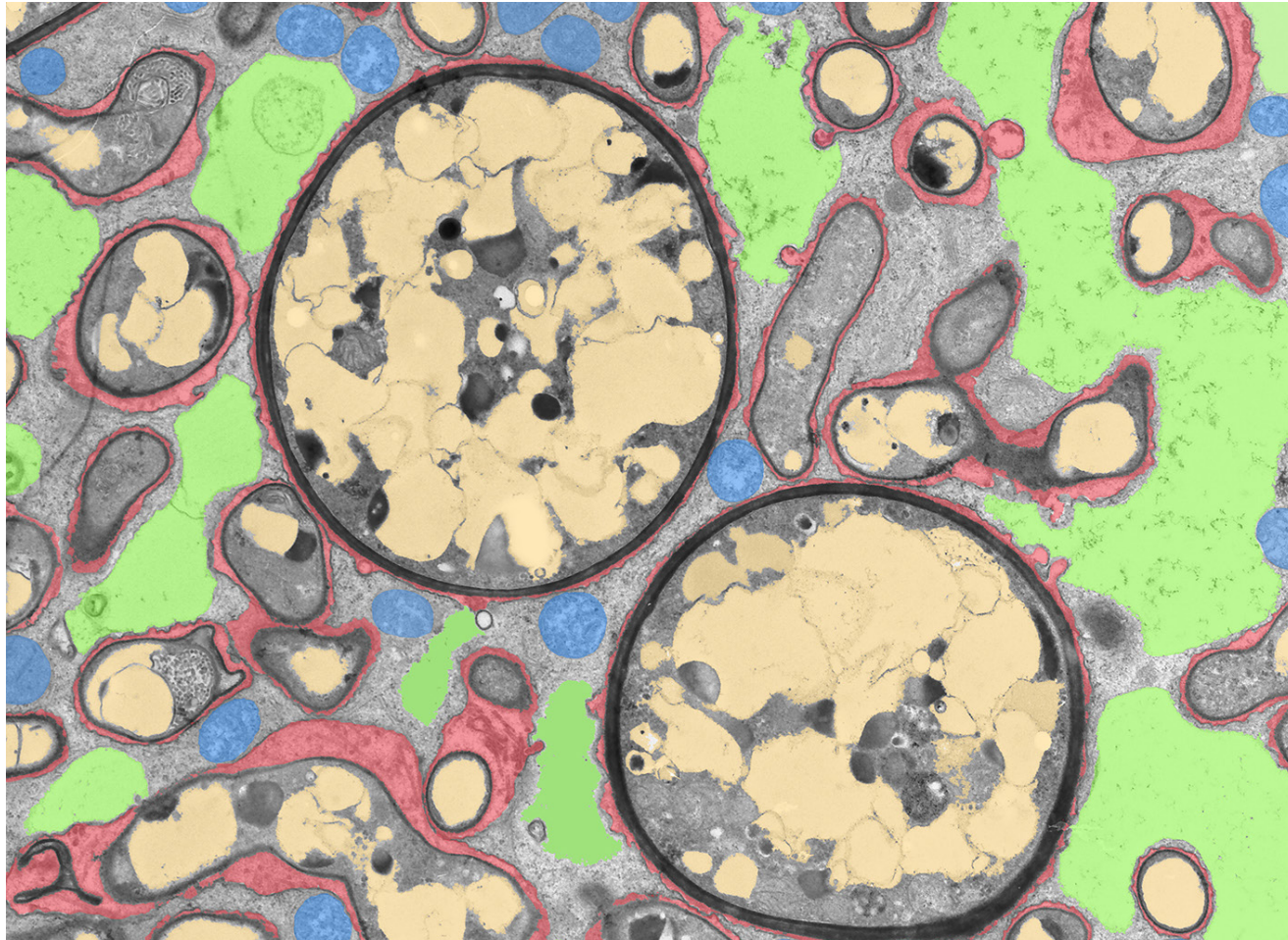


Figure 1 (Top) A root cell colonized by an arbuscule of an AM fungus.

Fungal hyphae are marked by their light brown vacuoles, the vacuoles of the host are in green, host mitochondria appear blue, and the symbiotic interface between the two partners is highlighted in red.

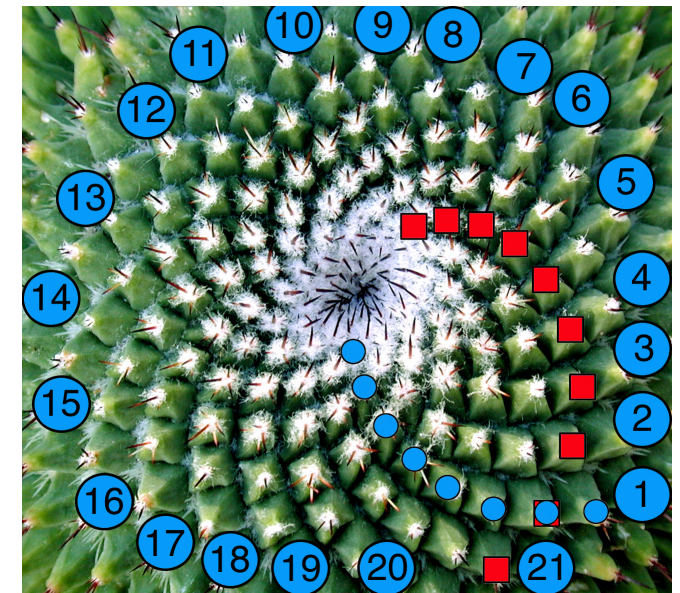
(Right) Fibonacci arrangement of organs of a cactus.

Spirals in clockwise and counterclockwise direction (parastichies) occur in numbers that reflect subsequent members in the Fibonacci series. This example has 13 clockwise parastichies and 21 counterclockwise parastichies. Members of the Fibonacci series reflect the sum of the two previous members.

Further Projects:

Besides the AM symbiosis, we are working on developmental aspects of plants, in particular organ formation at the shoot apical meristem and elongation growth of the embryonic stem, the hypocotyl. A major question is how the distribution of the plant hormone auxin controls the patterns or organ positioning (phyllotaxis) according to the Fibonacci series (see Figure 1, Right and Swiss TV report Einstein from August 27th 2015). In a recent study, we have used new laser ablation techniques to explore how auxin distribution is regulated.

SRF1 Einstein: <http://www.srf.ch/sendungen/einstein/mathe-in-der-krise-einstein-entdeckt-den-zauber-der-zahlen>





Dr Rudolf Rohr

Theoretical ecology
Ecological networks and biodiversity

How the architectures of ecological networks impact biodiversity?

The impressive richness of species in ecological communities has long motivated ecologists to explore how this diversity could be maintained. Species are not isolated but they interact inside ecological networks. It has been shown that these networks of interactions are not assembled at random, but that they exhibit particular architectures. Our work explores their architectures and the consequences for maintaining biodiversity.

We combine mathematical models and data sets to determine the effect of network architecture on biodiversity. We mainly base our approach on the concept of “structural stability”. Structural stability is a way of quantifying the disruption that an ecosystem can tolerate before any of its constituting species goes extinct. This concept has been introduced by the famous mathematician René Thom while studying morphogenesis. For instance, we have been working on determining how the architecture of mutualistic network, food-webs, and competition system modulates the conditions for coexistence. We also develop new statistical models aiming at inferring, reconstructing, and predicting ecological networks (and more generally any type of networks, e.g., social) based on species traits.

Co-workers

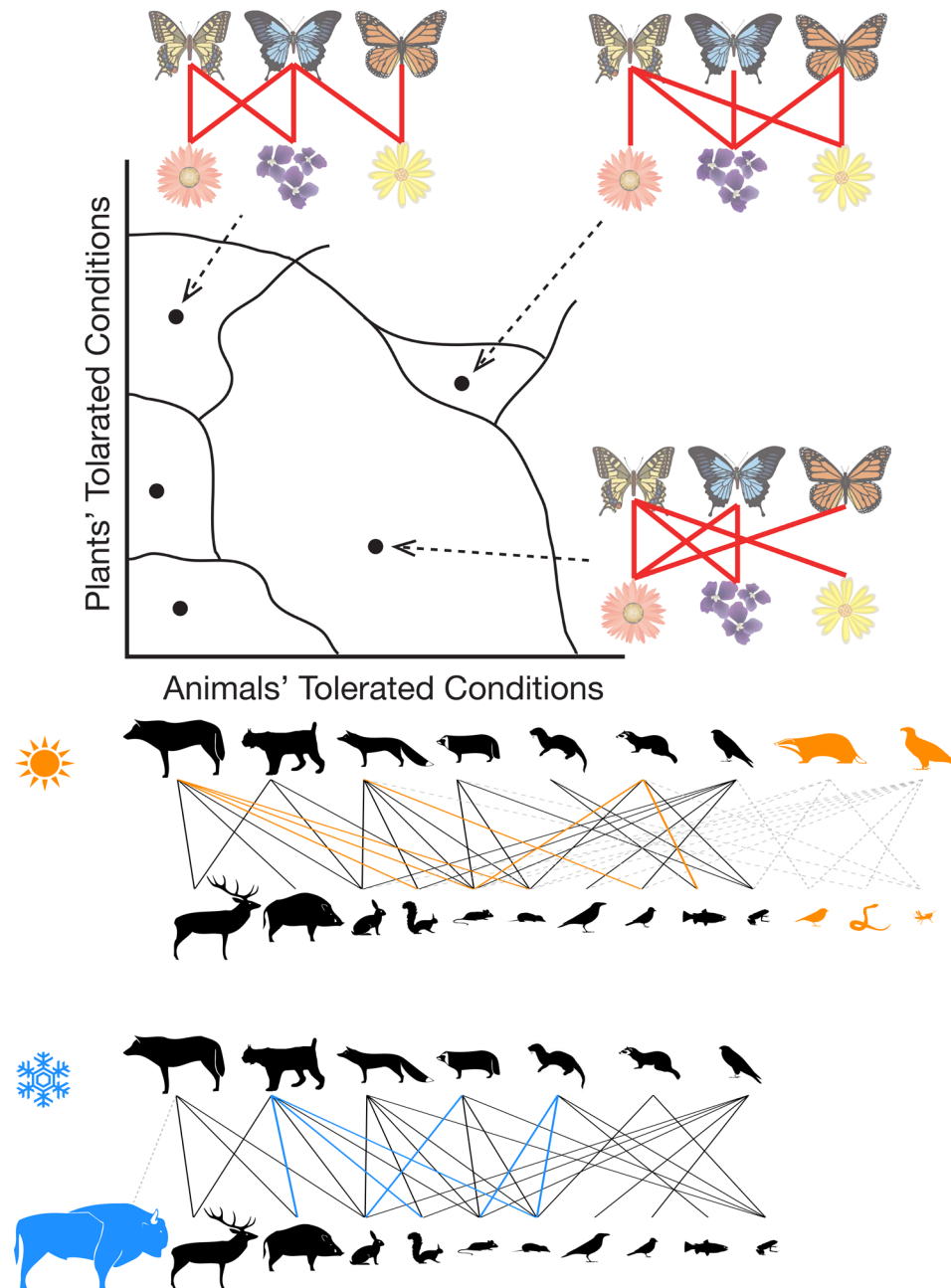
Prof. Roger Arditi, Prof. Louis-Félix Bersier, Dr Sarah Gray, Prof. Nicolas Loeuille, Prof. Christian Mazza, Prof. Serguei Saavedra

Selected publications

Rohr R.P. et al. (2014) On the structural stability of mutualistic systems. *Science* 345:1253497-1253497.

Saavedra S. et al. (2016) Seasonal species interactions minimize the impact of species turnover on the likelihood of community persistence. *Ecology* 97:865-873.

Rohr R. P. et al. (2016) Matching-centrality decomposition and the forecasting of new links in networks. *Proc. R. Soc. B* 283:20152702-20152702.



The figure illustrates how the conditions for maintaining biodiversity are modulated by the architecture of mutualistic network (e.g., plant-pollinator interactions). Our work shows that the nested architecture (bottom right network) of a plant-pollinator network allows a larger range of environmental conditions compatible with coexistence than a non-nested architecture (top networks). Figure from Rohr et al. (2014) *Science*

Illustration of turnover of species and their trophic interactions between summer and winter in the Białowieża primary forest. We show that the interaction turnover acts as a mechanism stabilizing the conditions of coexistence between the two seasons. Figure from Saavedra et al. (2016) *Ecology*.

How and where exactly are lipid droplets made ?



Prof. Roger Schneiter

Lipid homeostasis in yeast

Lipid droplets are found in most cell types, where they serve to store metabolic energy in form of fat (neutral lipids). This fatty core is covered by a phospholipid monolayer and harbors a specific set of proteins, many of which are implicated in lipid metabolism. Lipid droplets thus play important roles in obesity and insulin resistance. We have shown in the past, that these lipid droplets are closely associated with the membrane of the endoplasmic reticulum (ER), which is in contrast to the common belief that they would form cytosolic structures. However, whether these lipid droplets are actually attached to the surface of the ER, or whether they are within the luminal compartment could at that time not yet be resolved. To address this question, we developed a functional approach in which we targeted cytosolic, lipid droplet localized proteins into the ER lumen and determined, whether these proteins could still localize to lipid droplets. To our surprise, they do, indicating that lipid droplets are accessible from within the ER lumen, which challenges established model of lipid droplet biogenesis.

Co-workers

Dr Stéphanie Cottier, Rabi Khadwiche, Stefania de Angelis, Dr Mykhaylo Debelyy, Rasha Khaddaj, Dr Fernando Martínez-Montañés, Vendula Stradalova

Selected publications

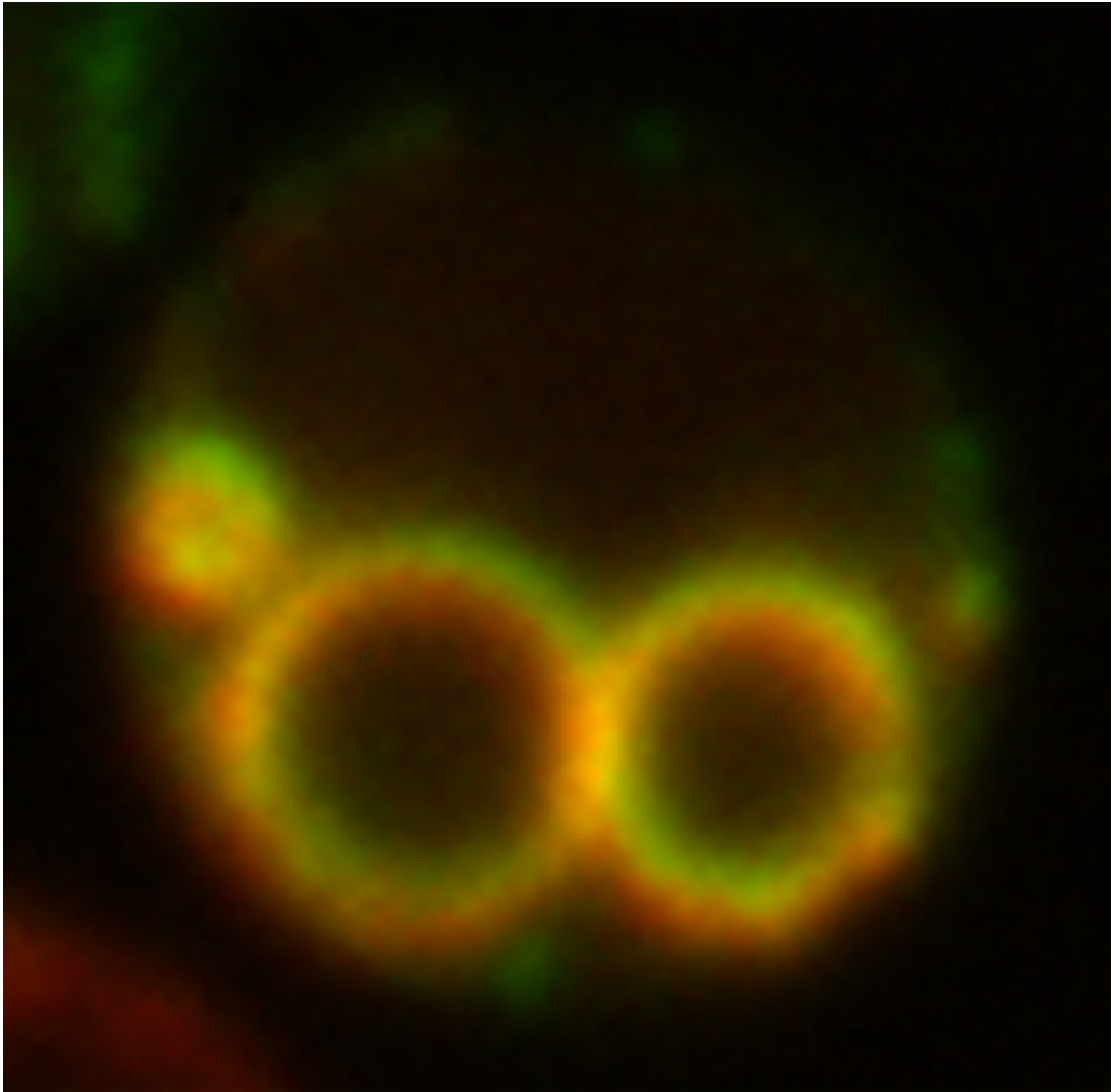
Martínez-Montañés, F., and Schneiter, R. (2016). Following the flux of long-chain bases through the sphingolipid pathway in vivo using mass spectrometry. *J. Lipid Research* 14, 906-15.

Darwiche, R., Kelleher, A., Hudspeth, E. M., Schneiter, R., Asojo, O. A. (2016) Structure and functional characterization of the CAP domain of pathogen-related yeast 1 (Pry1) protein. *Sci. Rep.* 6, 28838.

Mishra, S., Khaddaj, R., Cottier, S., Stradalova, V., Jacob, C., Schneiter, R. (2016). Lipid droplets are accessible to ER luminal proteins. *J. Cell Sci.* 129, 3803-15.

Mammalian perilipins localize to yeast LDs even when targeted to the ER lumen.

Colocalization of an ER lumenally targeted soluble lipid droplet protein, perilipin2 (green, GFP-PLIN2) and a cytosolic version of the same protein (red, mCherry-PLIN2). Wild-type (WT) yeast cells expressing the indicated fluorescent proteins were cultivated in media containing oleate and analyzed by confocal microscopy.





Prof. Simon Sprecher

Molecular, cellular and behavioural
neurobiology

How to make the brain work: Seeing, Tasting, Forgetting and building the right neurons

One of largest mysteries remains how our brain actually works. While science makes continuous progress towards this reaching this goal the complexity of the nervous system appears on first sight overwhelming. In particular with more than hundred billion neurons and a trillions of synaptic connections the human brain will remain a mystery despite rapid technical advances. Since the molecular and genetics nature of all nervous systems are shared among all animals the only way of understanding how the brain works is studying animal models with less complicated brains. In our laboratory we use the fruit fly as an impacting model system to understand various questions related to the brain.

How do cells know how to make up a complex nervous system?

The nervous system is without any doubt the most complex organ. How is such a complicated organ with thousands of highly interconnected cell types formed? How do cells know how they fit into this complex puzzle? We study the genetic and molecular mechanisms that control the fate of neurons. Using transcriptomics, molecular genetics and genome engineering we decipher the processes that allow neurons to diversify.

Co-workers

Yves Widmer, Cornelia Fritsch, Pauline Fritsch, Javier Bernardo-Garcia, Tim Humberg, Abhishek Mishra, Larisa Maier, Lucia de Andres, Marta Sprecher, Jules Duruz, Magali Jungo, Jasmin Abgottspon, Silvia Almeida, Clarisse Brunet

Selected publications

van Giesen L, Hernandez-Nunez L, ... , Sprecher SG. (2016) "Multimodal stimulus coding by a gustatory sensory neuron in *Drosophila* larvae." *Nature Communications*.

Bernardo-Garcia FJ, Fritsch C, Sprecher SG. (2016) "The transcription factor Glass links eye field specification with photoreceptor differentiation in *Drosophila*." *Development*. 15;143(8):1413-23.

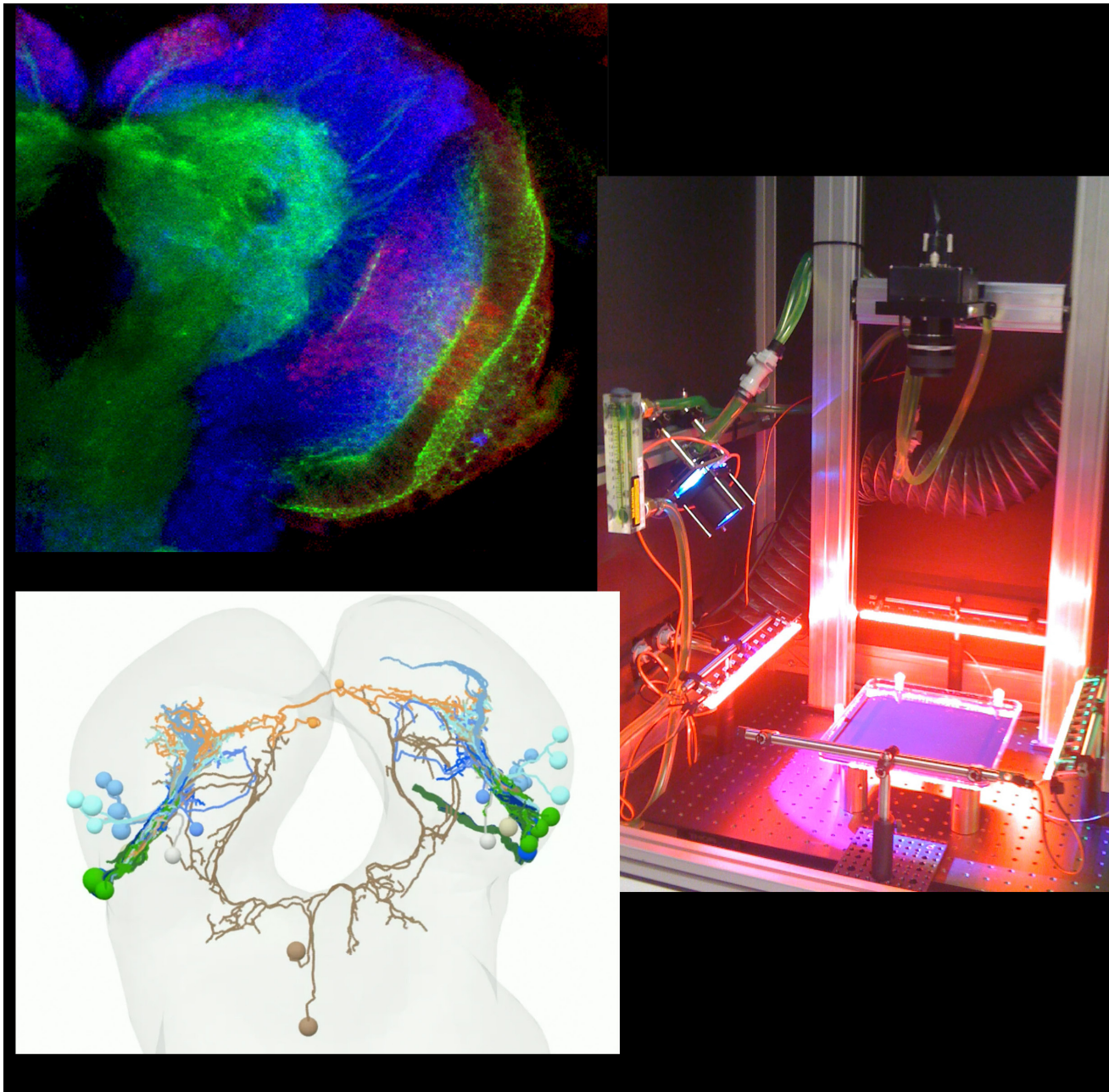
Klein M, Afonso B, ..., Sprecher SG, Gershow M, Garrity PA, Samuel AD.(2015) Sensory determinants of behavioral dynamics in *Drosophila* thermotaxis. *PNAS*. Jan 13;112(2):E220-9.

How does the nervous system perceive, integrate and process information from the environment?

We are constantly exposed to a wide range of sensory cues including light, odorants or tastants. Specialized sensory neurons perceive these cues and translate them into electrical signals, which in turn is translated into meaningful behavior by specific neuronal brain networks. But how does the brain integrate and process what our sensory systems experience? By studying the simple nervous system of the fruit fly larva we are able to tackle these questions. Genetically manipulating individual neurons and studying animal behavior by means of computer-aided analyses we decipher how brain function. We combine connectomics of circuits with functional imaging techniques understand activity within the network and the computation these circuits perform.

The logic of forgetting and its link to Alzheimers disease

While some memories are kept for years other memories are rapidly forgotten. However forgetting is not a passive, random process but underlies tightly controlled molecular machinery. Neurodegenerative diseases such as Alzheimers disease cause problems with the formation of memories or enhance the forgetting process. Studying the memory center of the fruit fly allows us to unveil these mechanisms.



Helping big data to set foot in the life sciences.



Prof. Daniel Wegmann

**Computational biology
and bioinformatics**

Many areas of biology are currently being fundamentally transformed by the advent of high-throughput technologies to accurately quantify and measure biological properties from the molecular and cellular level to whole organisms or ecosystems. The focus of our work is to develop novel statistical and computational tools such as machine learning to exploit the wealth of data being produced this way to help unraveling some of the biggest questions in modern biology.

A particular focus of our research this year was to incorporate Post Mortem Damage (PMD), a peculiar characteristics of DNA obtained from ancient samples, into bioinformatic and population genetic analyses. We developed new statistical tools to accurately infer genotypes and the genetic diversity of ancient samples that allowed us to learn more about the spread of farming and sedentism in prehistoric Europe, a radical change in human ecology was first invented 10,000 years ago in the Fertile Crescent.

By comparing ancient and modern samples from many corners of Europe, Anatolia and Iran we found that farming initially spread towards the Aegean only in terms of culture, not people, but from there into Western Europe predominantly through the colonization of people.

Co-workers

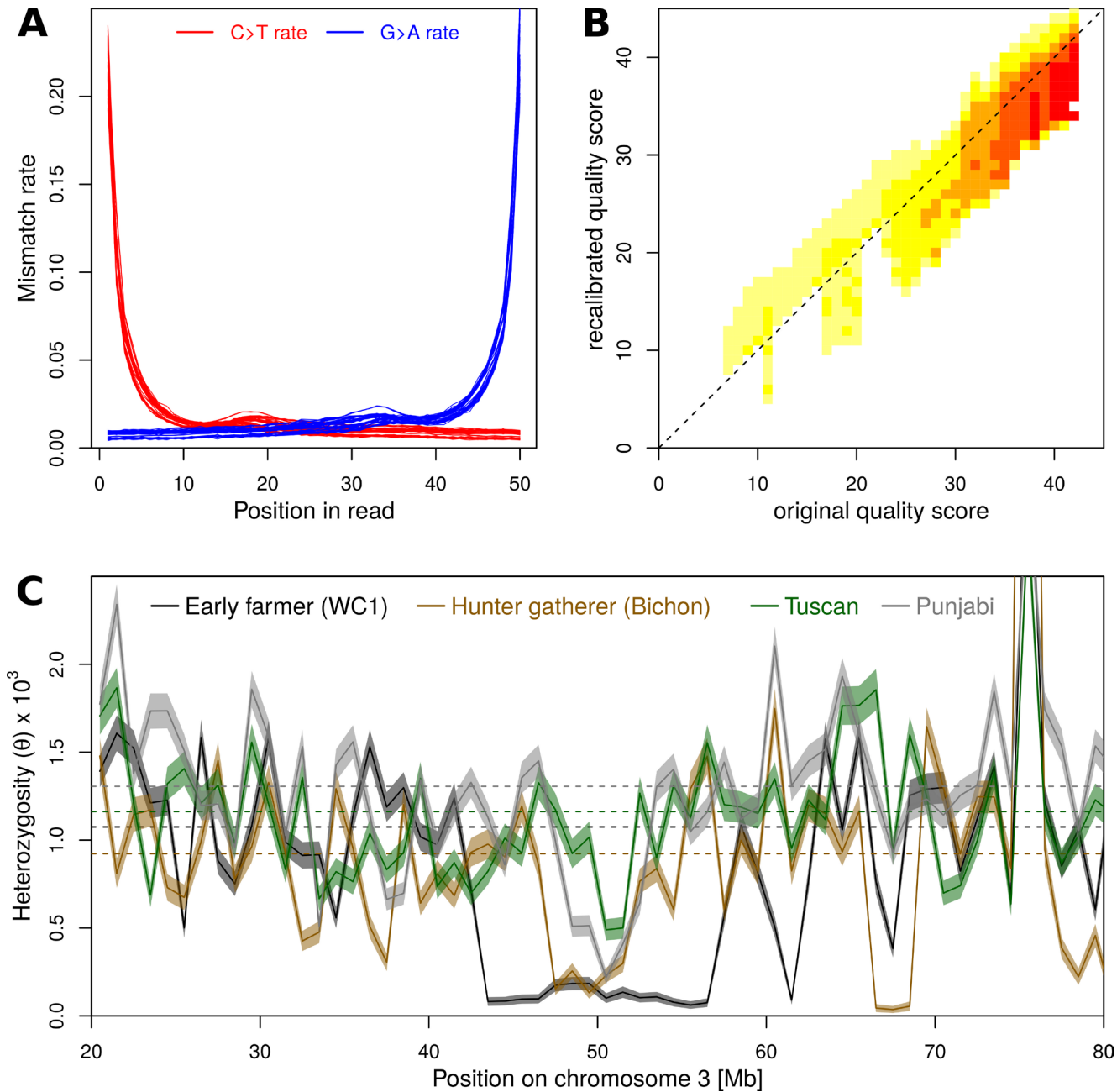
Thierry Aebischer, Pablo Duchon, Sara Foneca, Marco Galimberti, Vivian Link, Lorenz Rychener

Selected publications

Broushaki F et al. (2016). Early neolithic genomes from the eastern Fertile Crescent. *Science* 353: 499-503.

Hofmanová Z et al. (2016). Early farmers from across Europe directly descended from Neolithic Aegeans. *PNAS* 113: 6886-6891.

Kousathanas A et al. (2015). Likelihood-free inference in high-dimensional models. *Genetics* 203(2): 893-904.



The genetic diversity of the first farmers

Quantifying the genetic diversity of ancient samples such as WC1, an early farmers of the fertile crescent, is statistically challenging: the DNA suffered from post mortem damage (PMD) resulting in characteristic C to T and G to A changes at the ends of the sequencing reads (A), the data quality reported by the sequencing machine are biased, and the low amount of data renders genotyping uncertain. For this we developed the statistical framework ATLAS that accounts for PMD and genotyping uncertainty when recalibrating the quality scores (B) and inferring genetic diversity. For WC1, ATLAS revealed the genetic diversity to be intermediate to hunter gatherers and modern humans and to be distributed distinctly along the genome (C).



Dr Chantal Wicky

**Chromatin function
during development**

How is chromatin structure regulating development?

All processes in the nucleus of a cell take place in the context of chromatin, a complex of DNA and proteins. Chromatin is a very dynamic structure that can be altered by specialized enzymatic complexes, which in turn are modulating gene expression. The chromatin remodeler Mi2 functions in development and stem cell biology. Our lab is exploring its function using the nematode *C.elegans*, which presents many advantages for these studies: chromatin factors very similar to human, well characterized development and many useful molecular tools. Two Mi2 homologs are required for proper *C. elegans* development. One of them, LET-418 plays a role in postembryonic development. This process involves proliferation and differentiation of the stem cells, which allowed us to dissect functions of Mi2 in these very crucial biological processes. In the embryo, biochemical and genomic studies have revealed the teamwork of the two Mi2s, LET-418 and CHD-3 in fine-tuning chromatin composition at target genes involved in development. Our research aims at a better understanding of important epigenetic processes underlying development and stem cell biology.

Co-workers

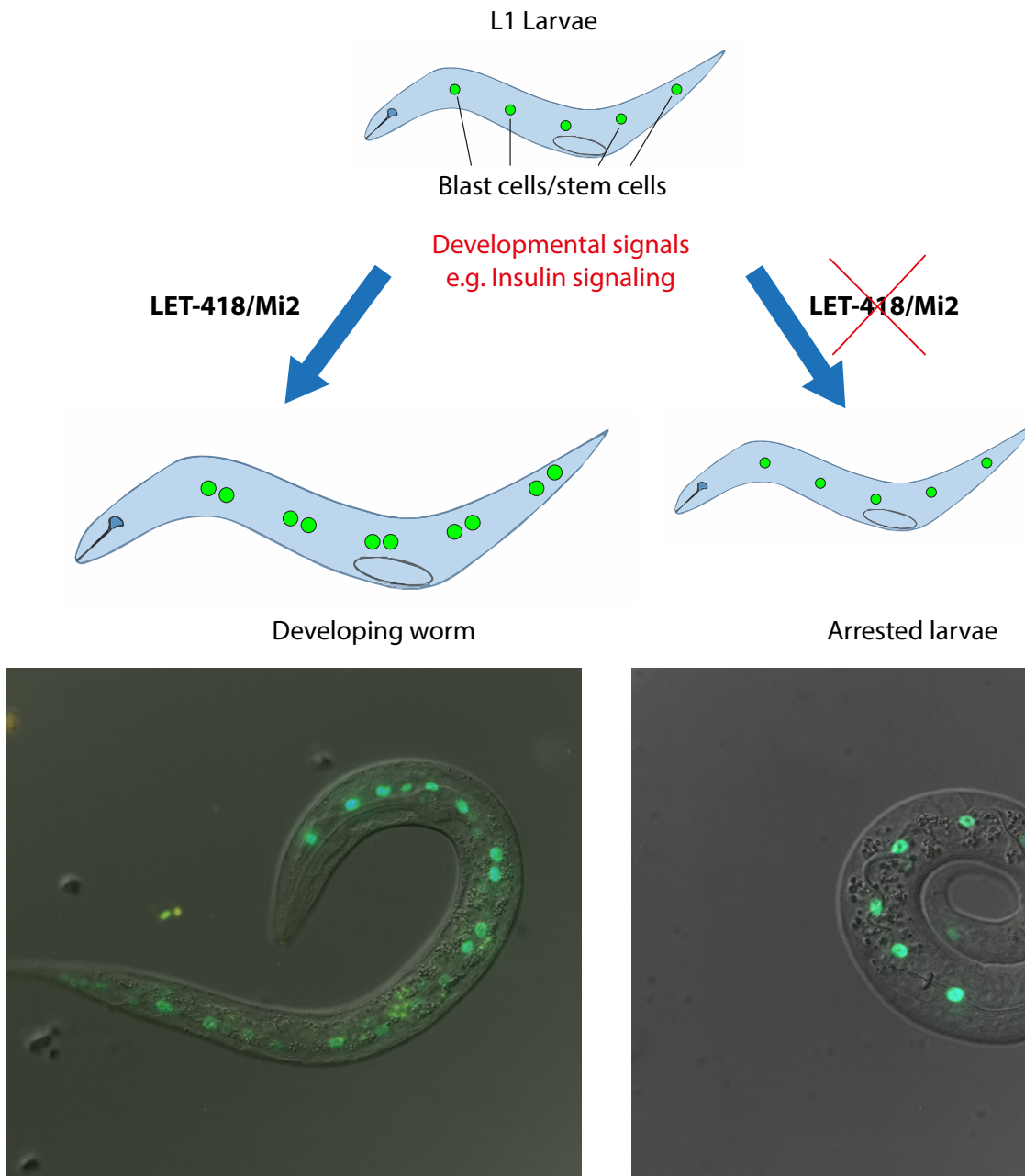
Stéphanie Käser-Pebernard, Caroline Aschinger, Makhabbat Saudenova, Peter Erdelyi, Marina Suleski, Laurence Bulliard and Fritz Müller.

Selected publications

Käser-Pebernard S et al. (2016). Fine-tuning of chromatin composition and Polycomb recruitment by two Mi2 homologues during *C. elegans* early embryonic development. *Epigenetics & chromatin* 9, 39.

Erdelyi P et al. (2017). A network of chromatin factors is regulating the transition to postembryonic development in *Caenorhabditis elegans* G3 (Bethesda) 7, 343.

Käser-Pebernard S et al. (2014). LET-418/Mi2 and SPR-5/LSD1 cooperatively prevent somatic reprogramming of *C.elegans* germline stem cells. *Stem Cell Reports* 2. DOI : 10.1016/j.stemcr.2014.02.007.



C. elegans larvae: “test tubes” for stem cell biology

We propose that LET-418/Mi2 together with other chromatin factors, are necessary to modulate chromatin structure in order to allow blast/stem cells to exit quiescence, to proliferate and to differentiate. Furthermore, our recent data indicates that the developmental function of LET-418/Mi2 depends on the insulin-signaling pathway.

Outreach activities

Lab2rue is our mobile lab that brings science to the public. We fascinated kids and adults with our little sniffer worm at the Explora day of our University and at the “Science on stage” fair in Winterthur. We are also training teachers to use *C. elegans* in the classrooms.





Albrecht's group



Bacher's group



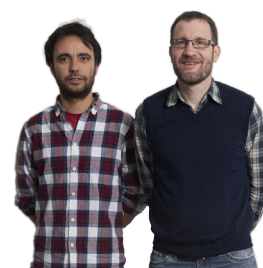
Bersier's group



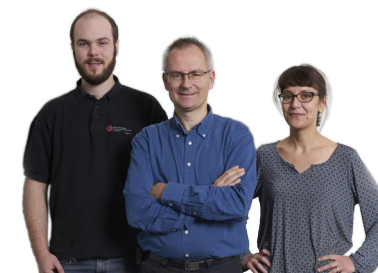
De Virgilio's group



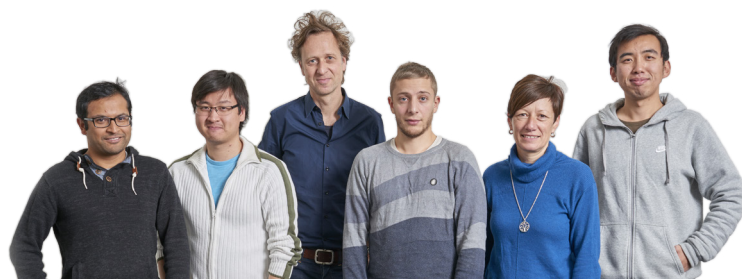
Dengjel's group



Egger's group



Falquet's group



Geisler's group



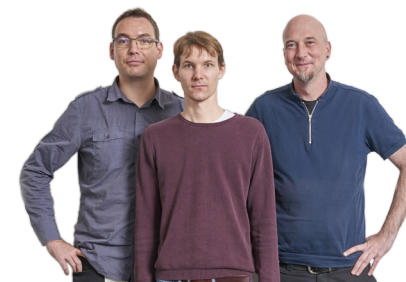
Glauser's group



Jacob's group



Jazvinska's group



Kressler's group



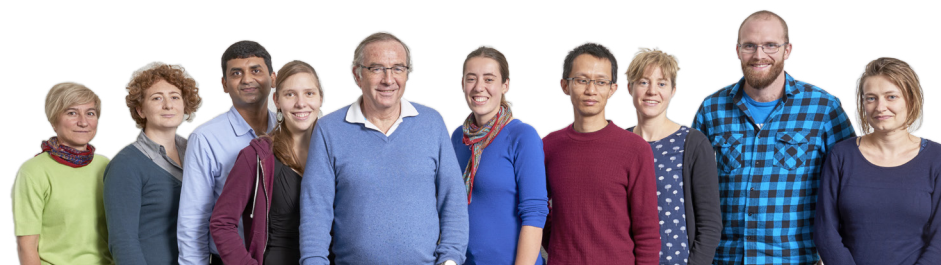
Kozlowski's group



Mauch's group



Mène-Safrané's group



Müller-schärer's group



Puoti's group



Reinhardt's group



Schneider's group



Sprecher's group



Wegmann's group



Wicky-Muller's group

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Technical service team



Comelli & apprentices



Secretary team

